Nanotechnology in Drug Delivery Systems: Current Trends and Future Perspectives

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ABSTRACT

Nanotechnology has emerged as a transformative approach in drug delivery systems, enhancing the efficacy and targeting of therapeutic agents. Current trends focus on the development of nanoparticles, liposomes, and dendrimers that can encapsulate drugs, improving their solubility and bioavailability. These nanocarriers are designed to release drugs in a controlled manner, allowing for sustained therapeutic effects while minimizing side effects. Moreover, the integration of targeting ligands on nanoparticles enables precise delivery to specific tissues or cells, such as cancerous tumors, thereby improving treatment outcomes and reducing systemic toxicity. Recent advancements in nanotechnology have also led to the exploration of stimuliresponsive systems that release drugs in response to environmental triggers, such as pH changes or temperature variations, further enhancing the specificity of drug delivery. Looking ahead, the future of nanotechnology in drug delivery systems holds immense potential for personalized medicine and advanced therapeutic

strategies. Researchers are exploring the use of nanotechnology to deliver RNA-based therapies, such as mRNA vaccines and gene editing tools, which require sophisticated delivery mechanisms to ensure stability and efficacy. Additionally, the combination of nanotechnology with artificial intelligence and machine learning is paving the way for the design of smart drug delivery systems that can adapt to patient-specific needs in real-time. Regulatory challenges and safety concerns regarding the use of nanomaterials must be addressed to facilitate their clinical translation. Overall, the ongoing research and innovation in nanotechnology promise to revolutionize drug delivery, making treatments more effective and tailored to individual patient profiles.

KEYWORDS: Nanotechnology, Drug delivery systems, Nanoparticles, Liposomes, Dendrimers, Controlled release, Targeted therapy, Stimuli-responsive systems, Personalized medicine, RNA-based therapies, Artificial intelligence, Regulatory challenges, Clinical translation.

1. Introduction

Nanotechnology, the manipulation of matter on an atomic and molecular scale, has emerged as a transformative field with profound implications across various sectors, particularly in medicine. One of the most promising applications of nanotechnology is in drug delivery systems (DDS), where it offers innovative solutions to longstanding challenges in pharmacology, such as drug solubility, stability, bioavailability, and targeted delivery. As the global burden of diseases continues to rise, particularly chronic conditions such as cancer, diabetes, and cardiovascular diseases, the need for more effective and efficient drug delivery mechanisms becomes increasingly critical. This essay aims to explore the current trends in nanotechnology-based drug delivery systems, highlighting their mechanisms, advantages, and challenges, while also discussing future perspectives that could shape the landscape of pharmaceutical therapies [1].

The concept of nanotechnology dates back to the early 1980s, but its application in medicine began gaining momentum in the late 1990s with the advent of nanomedicine. Nanomedicine encompasses the use of nanotechnology for diagnosis, prevention, and treatment of diseases. In drug delivery, nanoparticles—ranging from 1 to 100 nanometers in size—serve as carriers for therapeutic agents, enhancing their pharmacological properties and enabling more precise targeting of disease sites. The unique physicochemical properties of nanoparticles, including their large surface area-to-volume ratio, tunable size, and ability to encapsulate various types of drugs, make them particularly suitable for improving drug delivery [2]. Current Trends in Nanotechnology-Based Drug Delivery Systems

Recent advancements in nanotechnology have led to the development of various drug delivery systems that can be categorized based on their composition and mechanism of action. Liposomes, dendrimers, polymeric nanoparticles, and inorganic nanoparticles are among the most widely studied nanocarriers. Each type presents unique benefits and challenges, contributing to the ongoing evolution of DDS [3].

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1.   Liposomes: These spherical vesicles composed of phospholipid bilayers are one of the earliest forms of nanocarriers. They can encapsulate both hydrophilic and hydrophobic drugs, enhancing their solubility and stability. Liposomes have been successfully used in the delivery of chemotherapeutic agents, with formulations like Doxil® demonstrating improved therapeutic efficacy and reduced side effects in cancer treatment.

2.   Polymeric Nanoparticles: These are composed of biodegradable polymers that can provide controlled release of drugs over extended periods. Their ability to be engineered for specific release profiles makes them ideal for chronic disease management. Recent studies have focused on using stimuli-responsive polymers that release drugs in response to environmental triggers, such as pH or temperature changes, thereby enhancing the precision of drug delivery.

3.   Dendrimers: These highly branched, tree-like macromolecules offer a high degree of functionalization and versatility. Dendrimers can be tailored to carry multiple drug molecules, allowing for combination therapies that target different pathways in disease progression. Their uniform size and shape facilitate predictable pharmacokinetics, making them a valuable tool in personalized medicine.

4.   Inorganic Nanoparticles: Gold, silver, and silica nanoparticles have gained attention due to their unique optical and electronic properties. They can be used for both drug delivery and imaging, providing a dual function that enhances diagnostic and therapeutic capabilities. For example, gold nanoparticles can be conjugated with drugs and targeted to cancer cells, where they can release the drug upon exposure to specific wavelengths of light [4].

Advantages of Nanotechnology in Drug Delivery

The integration of nanotechnology into drug delivery systems offers numerous advantages over traditional methods. Firstly, nanocarriers enhance the bioavailability of poorly soluble drugs, a common challenge in pharmaceutical development. By improving solubility and stability, nanoparticles can facilitate the absorption of drugs in the gastrointestinal tract or through biological membranes [5].

Secondly, targeted drug delivery is significantly improved with the use of nanoparticles. By modifying the surface properties of nanocarriers, researchers can achieve selective targeting of diseased tissues, minimizing systemic exposure and reducing side effects. This is particularly crucial in cancer therapy, where conventional treatments often harm healthy tissues along with tumor cells [5].

Finally, the ability to control the release of drugs through nanotechnology allows for sustained therapeutic effects and improved patient compliance. Controlled release systems can reduce the frequency of dosing, leading to better adherence to treatment regimens [5].

Despite the promise of nanotechnology in drug delivery, several challenges remain. One major concern is the potential toxicity of nanoparticles, which can arise from their

size, shape, and surface chemistry. Understanding the biocompatibility and long-term effects of nanocarriers is essential for their safe application in humans [6].

Moreover, the scalability of nanotechnology-based drug delivery systems poses significant hurdles. While laboratory-scale synthesis and characterization of nanoparticles may yield promising results, translating these findings into commercial products requires overcoming regulatory and manufacturing challenges [6].

Looking ahead, the future of nanotechnology in drug delivery systems is bright, with several trends poised to shape its development. Personalized medicine, which tailors treatment to individual patient profiles, is likely to benefit significantly from advancements in nanotechnology. By utilizing patient-specific data, such as genetic information, researchers can design nanoparticles that deliver drugs more effectively based on the unique characteristics of a patient's disease [7].

Furthermore, the integration of artificial intelligence (AI) and machine learning in the design and optimization of nanocarriers is expected to accelerate the discovery of new drug delivery systems. These technologies can analyze vast datasets to predict the behavior of nanoparticles in biological systems, enhancing the efficiency of drug development [7].

Finally, the ongoing research into combination therapies, where multiple therapeutic agents are delivered simultaneously using nanocarriers, holds great promise for treating complex diseases. This approach could lead to synergistic effects, improving treatment outcomes and reducing the likelihood of drug resistance [7]. Mechanisms of Nanoparticle Drug Delivery: Principles and Techniques:

The field of drug delivery has witnessed transformative advancements over recent decades, particularly with the advent of nanotechnology. Nanoparticle drug delivery systems, which leverage particles in the nanometer size range (1-100 nm), offer unprecedented ways to optimize therapeutic delivery, enhance bioavailability, reduce side effects, and improve patient outcomes. This essay delves into the mechanisms of nanoparticle drug delivery, highlighting the principles that govern their design and functionality, as well as the various techniques employed in this burgeoning area of biomedical research [8].

Fundamentals of Nanoparticle Drug Delivery

Nanoparticle Characteristics

Nanoparticles can be composed of a variety of materials, including lipids, polymers, metals, and silica, each conferring unique properties that can be tailored for specific applications. The characteristics of nanoparticles that influence drug delivery include:

1.   Size: The size of nanoparticles plays a crucial role in their biodistribution and cellular uptake. Generally, smaller nanoparticles (less than 100 nm) can more readily extravasate through leaky vasculature found in tumors or inflamed tissues, a principle known as the Enhanced Permeability and Retention (EPR) effect [9].

2.   Shape and Morphology: The surface area-to-volume ratio and shape of nanoparticles can significantly affect their interaction with biological systems.

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Spherical nanoparticles, for example, tend to exhibit improved circulation times compared to their non-spherical counterparts, leading to enhanced therapeutic efficacy [9].

3.   Surface Modifications: Functionalization of nanoparticle surfaces with ligands or targeting moieties can enhance their specificity towards disease sites. For instance, attaching antibodies or peptides that selectively bind to markers on tumors can facilitate targeted drug delivery, minimizing off-target effects [10].

Mechanisms of Drug Release

The release of therapeutics from nanoparticles can occur through several mechanisms:

1.   Diffusion: The most common release mechanism in polymer-based nanoparticles, diffusion allows drugs to escape based on concentration gradients.

2.   Degradation: Some nanoparticles are designed to degrade in response to physiological conditions, such as pH or enzymatic activity. For example, biodegradable polymers can gradually break down, releasing their payload over time.

3.   External Stimuli: Smart nanoparticles can be engineered to release their drugs in response to external stimuli, such as magnetic fields, temperature changes, or light. These "on-demand" release systems enable precise control over drug delivery [11].

Techniques in Nanoparticle Drug Delivery

The successful application of nanoparticles in drug delivery relies on various techniques for their synthesis, characterization, and delivery. Below are some of the key methodologies: Synthesis Techniques

1.   Solvent Evaporation: This is a common technique for creating polymeric nanoparticles, wherein a drug-loaded polymer solution is prepared and then the solvent is evaporated, leading to particle formation. This method is advantageous for encapsulating hydrophobic compounds [12].

2.   Emulsion Polymerization: Another prevalent method, emulsion polymerization creates nanoparticles through the polymerization of monomers in the presence of surfactants, forming stable dispersions. This technique enables precise control over particle size and distribution [12].

3.   Nanoprecipitation: In this approach, a drug is dissolved in a solvent that is miscible with water, and upon adding it to an aqueous phase, the drug precipitates to form nanoparticles. It is especially useful for drug formulations requiring rapid and efficient loading [12].

Characterization Techniques

Characterizing nanoparticles is vital for assessing their quality and performance. Common characterization techniques include:

1.	Dynamic Light Scattering (DLS): This method measures particle size distribution by analyzing scattering patterns of light emitted from illuminated nanoparticles in suspension.

2.	Transmission Electron Microscopy (TEM): TEM provides detailed images of the morphology and size of nanoparticles, revealing structural information at nanometer resolution.

3.	Surface Charge Measurement: Zeta potential analysis is used to determine the stability of nanoparticles in suspension, as surface charge influences interaction with biological systems and cellular uptake [13].

Drug Delivery Techniques

1.	Intravenous Injection: This is the most straightforward approach, allowing for rapid systemic distribution of nanoparticles. Careful consideration of particle size and surface properties is necessary to facilitate efficient circulation and delivery [14].

2.	Targeted Delivery Approaches: By conjugating nanoparticles with targeting ligands, such as antibodies or other biomolecules, researchers can enhance the specificity of drug delivery. The binding of these ligands to their particular receptors on target cells can promote cellular uptake and increase therapeutic efficacy [14].

3.	Localized Delivery: Nanoparticles can also be administered directly to the site of action, such as tumors, through surgical implantation or injection. This minimizes systemic exposure and potential side effects [15].

Current Applications and Future Perspectives

Nanoparticle drug delivery systems have shown promise across various therapeutic areas, including oncology, cardiovascular diseases, and vaccination. For instance, liposomal formulations and nanocrystals have been widely adopted for cancer therapy, improving the solubility and distribution of chemotherapeutics while reducing toxicity [16].

As the field evolves, several trends are emerging. Personalized medicine, where treatment is tailored to individual patient profiles, is becoming increasingly feasible with nanoparticle-based systems. Moreover, the integration of artificial intelligence and machine learning for drug design and characterization is anticipated to expedite the development of more effective therapeutic nanoparticles [16].

Current Trends in Nanocarrier Development:

Nanocarriers have emerged as a pivotal innovation in the field of drug delivery and biomedical applications. These nanoscale vehicles, which can transport therapeutic agents directly to targeted cells or tissues, are designed to enhance the efficacy and safety of treatments while minimizing side effects. The integration of nanotechnology into medicine has paved the way for significant advancements in how drugs are delivered, particularly for cancer therapies, gene delivery, and vaccine development.

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This essay explores the current trends in nanocarrier development, focusing on materials, design strategies, applications, and regulatory considerations [17].

1. Materials for Nanocarriers

The choice of materials for nanocarriers is fundamental to their function and effectiveness. Currently, several classes of materials are being explored, each with unique properties that can be tailored for specific applications.

Lipid-based nanocarriers, such as liposomes and solid lipid nanoparticles (SLNs), are among the most widely studied types. Liposomes, which are spherical vesicles composed of lipid bilayers, can encapsulate both hydrophilic and hydrophobic drugs. Recent trends in this area include the development of targeted liposomes that can selectively bind to specific cell types, improving drug delivery precision. For instance, the incorporation of ligands such as antibodies or peptides can enhance the targeting capabilities of liposomes, allowing for the preferential delivery of chemotherapeutic agents to tumor cells [18]

Polymeric nanoparticles are another major category of nanocarriers, offering versatility in drug loading and release profiles. Biodegradable polymers, such as polylactic-co-glycolic acid (PLGA) and chitosan, are particularly popular due to their biocompatibility and ability to degrade into non-toxic byproducts. Recent advancements have focused on the development of stimuli-responsive polymeric nanocarriers that can release their payloads in response to specific environmental triggers, such as pH, temperature, or enzymatic activity. This approach allows for controlled and localized drug release, enhancing therapeutic effectiveness [18].

Inorganic nanocarriers, including silica nanoparticles, gold nanoparticles, and magnetic nanoparticles, are gaining traction due to their unique optical and magnetic properties. Gold nanoparticles, for example, can be used for photothermal therapy, where they absorb light and convert it into heat to destroy cancer cells. Silica nanoparticles can be engineered for drug delivery and imaging applications, providing dual functionality. The use of magnetic nanoparticles allows for targeted delivery using external magnetic fields, enabling precise localization of therapeutic agents at the desired site [19].

2. Design Strategies

The design of nanocarriers is crucial for optimizing their performance in drug delivery applications. Current trends emphasize the importance of customizing the physicochemical properties of nanocarriers to enhance their stability, circulation time, and cellular uptake.

Surface modification of nanocarriers is a key strategy for improving their interaction with biological systems. By altering the surface characteristics—such as charge, hydrophilicity, and functionalization—researchers can enhance the biocompatibility and targeting ability of nanocarriers. For example, PEGylation, the process of attaching polyethylene glycol (PEG) chains to the surface of nanoparticles, is widely

used to increase circulation time in the bloodstream and reduce immune recognition. This modification helps to evade the reticuloendothelial system (RES), allowing for prolonged systemic availability of the drug [20].

The development of multifunctional nanocarriers that can perform multiple tasks simultaneously is an exciting trend in nanocarrier design. These carriers can be engineered to deliver therapeutic agents while also providing imaging capabilities or facilitating real-time monitoring of drug release. For instance, nanoparticles can be loaded with both a chemotherapeutic drug and a fluorescent dye, allowing for simultaneous treatment and visualization of the therapeutic effect. This multifunctionality enhances the overall efficacy of treatment and provides valuable insights into the pharmacokinetics of the delivered drug [20].

3. Applications in Medicine

The applications of nanocarriers in medicine are vast and continually expanding. Current trends indicate a strong focus on oncology, gene therapy, and vaccine development [21].

Nanocarriers have shown remarkable promise in cancer therapy by enabling targeted drug delivery, reducing off-target effects, and overcoming drug resistance. Recent advancements include the development of nanocarrier systems that can co-deliver multiple drugs to synergistically enhance treatment outcomes. Additionally, the use of nanocarriers in combination with immunotherapy is an emerging trend, as they can help deliver immune-modulating agents directly to tumor sites, thereby boosting the body's immune response against cancer cells [21].

Gene therapy is another area where nanocarriers are making significant contributions. The ability to deliver nucleic acids, such as DNA and RNA, to specific cells is essential for the success of gene therapies. Nanocarriers, particularly lipid nanoparticles, have been instrumental in the delivery of mRNA vaccines, as seen in the rapid development of COVID-19 vaccines. Researchers are now exploring the use of nanocarriers for delivering CRISPR/Cas9 systems for gene editing, which could revolutionize the treatment of genetic disorders [22].

The COVID-19 pandemic highlighted the potential of nanocarriers in vaccine development. Lipid nanoparticles were employed in the mRNA vaccines, facilitating the safe delivery of mRNA into cells. Current trends indicate ongoing research into using nanocarriers for developing next-generation vaccines, including those targeting infectious diseases and cancer. The ability to enhance immune responses through targeted delivery of antigens or adjuvants using nanocarriers is a promising area of investigation [23].

4. Regulatory Considerations

As the field of nanocarrier development progresses, regulatory considerations become increasingly important. The unique properties of nanocarriers pose challenges in terms of safety and efficacy evaluation. Regulatory agencies, such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), are actively working to establish guidelines for the assessment of nanomedicines. Current trends

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indicate a move towards more comprehensive frameworks that address the specific challenges associated with nanotechnology, including characterization, manufacturing, and pharmacokinetics [24].

The safety and toxicity of nanocarriers are critical concerns that must be addressed before clinical applications. Current research is focused on understanding the interactions between nanocarriers and biological systems, including their biodistribution, metabolism, and potential toxicity. Studies are being conducted to evaluate the long-term effects of nanocarrier administration and to establish safe dosage ranges [24].

Standardization and quality control are essential for ensuring the reproducibility and reliability of nanocarrier products. Current trends emphasize the need for standardized protocols for the characterization of nanocarriers, including size, shape, surface properties, and drug loading capacity. Regulatory agencies are working towards developing guidelines that will facilitate the approval process for nanomedicines, ensuring that they meet stringent safety and efficacy standards [25].

Targeted Drug Delivery: Enhancing Efficacy and Reducing Toxicity:

In recent decades, medical research has increasingly focused on the development of targeted drug delivery systems (TDDS)—a novel approach aimed at enhancing the therapeutic efficacy of medications and minimizing their systemic toxicity. The traditional model of drug administration often results in significant side effects due to non-specific distribution throughout the body. Targeted drug delivery, on the other hand, seeks to direct drugs to specific tissues or cells, thus concentrating therapeutic effects where they are needed most while reducing exposure to healthy tissues. This essay delves into the fundamental principles of targeted drug delivery, its various methods and technologies, its applications in different fields of medicine, and the challenges and future directions for this transformative approach [25].

Targeted drug delivery systems are designed to release therapeutics at precise locations within the body. The rationale behind this approach stems from the observation that conventional drug administration methods—such as oral, intramuscular, or intravenous routes—often disperse the active compounds throughout the entire body. As a result, therapeutic agents can interact with unintended targets, leading to adverse side effects that compromise patient safety and adherence to treatment regimens [26].

At the core of targeted drug delivery is a strategy that employs carrier systems capable of encapsulating drugs and delivering them specifically to diseased tissues or cells. These systems can be engineered to respond to certain physiological signals, such as pH, temperature, or biomarkers specific to certain diseases, thus allowing for a controlled release of the therapeutic agent. The two primary goals of targeting drug delivery are to increase local drug concentration at the disease site (enhancing efficacy) and to lessen the side effects associated with systemic exposure (reducing toxicity) [27].

Strategies for Targeted Drug Delivery

Several strategies for targeted drug delivery have emerged, including passive targeting, active targeting, and stimuli-responsive systems [28].

1.   Passive Targeting: This approach relies on physiological differences between healthy and diseased tissues. For instance, tumors often have leaky vasculature and impaired lymphatic drainage, which can lead to the accumulation of nanoparticles or liposomes in tumor sites, a phenomenon known as the Enhanced Permeability and Retention (EPR) effect. This passive approach can enhance local drug delivery simply by exploiting the unique vascular characteristics of tumors [28].

2.   Active Targeting: Unlike passive targeting, which depends solely on the physical and biological characteristics of tissues, active targeting employs ligands—molecules that bind specifically to certain receptors on the surface of target cells. By attaching ligands such as antibodies, peptides, or small molecules to the surface of drug carriers, researchers can increase the specificity of drug delivery. This technique is particularly useful in oncology, where cancer cells often express unique biomarkers that can be targeted [29].

3.   Stimuli-Responsive Systems: These innovative systems release drugs in response to specific stimuli in the body, such as changes in pH, temperature, or the presence of certain enzymes. For example, drug-loaded nanoparticles might remain inert at normal body conditions but release their contents when they encounter the acidic microenvironment of a tumor. This targeted approach increases the precision of therapy while minimizing drug presence in the circulation [29].

Applications in Medicine

Targeted drug delivery has made significant strides in various medical fields, particularly in oncology, cardiovascular treatments, and the management of chronic diseases.

1.   Oncology: Cancer treatment has arguably benefited the most from advances in targeted drug delivery. Conventional chemotherapeutic agents are notorious for causing severe side effects, including nausea, hair loss, and immunosuppression. By using liposomes or polymer-based nanocarriers that can encapsulate chemotherapeutics, researchers have demonstrated improved therapeutic indices. For instance, the development of liposomal doxorubicin has improved delivery to tumors while minimizing cardiotoxicity [30].

2.   Cardiovascular Health: Targeted drug delivery systems are also being explored for cardiovascular applications, such as localized delivery of anti-inflammatory agents to atheromatous plaques in the arterial walls. This targeted approach aims to prevent plaque rupture and resultant myocardial infarctions by directly administering therapeutic agents to sites of vascular inflammation [30].

3.   Chronic Diseases: In chronic diseases, such as diabetes, targeted delivery systems are being developed to provide sustained release of medications like insulin, which could enhance patient compliance and improve glycemic control.

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Biodegradable microspheres or hydrogels that release insulin in response to glucose levels in the blood offer a tantalizing prospect for smarter and more effective diabetes management [31].

Challenges and Future Directions

While the potential of targeted drug delivery is immense, several challenges remain. One of the primary obstacles is the complexity of human tissues and organs. Achieving precise targeting requires an in-depth understanding of the interactions between drug carriers and biological systems. Moreover, regulatory hurdles often pose significant barriers to the clinical translation of innovative drug delivery systems [31] .

Another challenge lies in the potential development of resistance. For instance, cancer cells can alter their surface markers, leading to reduced efficacy of active targeting systems. This necessitates ongoing research to dynamically address changes in the microenvironment and modify drug carriers accordingly [32].

Future directions for targeted drug delivery include the development of multifunctional platforms capable of delivering combinations of drugs, imaging, and diagnostic capabilities—essentially creating theranostic systems. Additionally, advancements in nanotechnology and materials science will likely contribute to improved targeting and efficacy [32].

Stimuli-Responsive Drug Delivery Systems: Innovations and Applications:

The field of drug delivery has witnessed significant advancements in recent years, spurred by the burgeoning understanding of nanotechnology, materials science, and biological interactions. Among these advancements, stimuli-responsive drug delivery systems (SRDDS) stand out as an innovative approach that allows for controlled and targeted release of therapeutics based on specific environmental triggers. These systems not only promise enhanced therapeutic efficacy and reduced systemic toxicity but also open new avenues for personalized medicine. This essay delves into the underlying principles of SRDDS, reviews the innovative materials and mechanisms employed, and explores their diverse applications in medicine [33].

Stimuli-responsive drug delivery systems refer to smart drug carriers that respond to external stimuli—such as pH, temperature, light, magnetic fields, or biochemical signals—to modulate the release of drugs. Traditional drug delivery methods often suffer from limitations such as poor bioavailability, lack of specificity, and adverse side effects due to systemic distribution. In contrast, SRDDS aim to overcome these challenges by ensuring that the drug is released in a controlled fashion, contingent upon the presence of specific triggers. This responsiveness is typically achieved through the use of specially designed polymers or nanocarriers that can alter their properties in response to these stimuli [34].

The design principle of SRDDS can broadly be classified based on the type of stimulus. pH-responsive systems are particularly prevalent due to the vastly different pH levels found in various biological compartments. For example, the acidic environment of

tumors compared to normal tissues can be exploited for targeted drug release. Temperature-responsive systems utilize phase transition properties of certain hydrogels, which can change from gel to liquid state at physiological temperatures, allowing for localized therapy. Light-responsive systems can deliver drugs in precise doses through photo-cleavable linkers, beneficial for applications that require spatial confinement, such as local cancer therapies [35].

A significant component of SRDDS development involves innovative materials fabrication. Various biocompatible polymers such as poly(lactic-co-glycolic acid) (PLGA), poly(N-isopropylacrylamide) (PNIPAAm), and chitosan have been engineered for specific responsive characteristics. Particularly, PNIPAAm is known for its lower critical solution temperature (LCST) behavior, wherein it remains soluble in aqueous media at lower temperatures but precipitates at higher temperatures. This property can be harnessed for temperature-sensitive drug delivery applications [36].

Nanoparticles, hydrogels, and microcapsules are common carriers employed in SRDDS. For instance, liposomes can be engineered to respond to specific enzyme levels, which are elevated in certain diseases, enabling the release of encapsulated drugs in pathological conditions. Additionally, advancements in the field of inorganic nanoparticles have allowed for the integration of multiple stimuli, such as magnetic fields and ultrasound, enhancing the versatility of drug delivery systems [37].

Moreover, the incorporation of bioactive signaling molecules such as peptides or antibodies into these systems has also gained traction. These bioconjugates can provide a dual function, responding to external stimuli while also guiding the system to specific cell types, enhancing targeting capabilities. This multifaceted approach signals a shift towards smarter and more comprehensive treatment modalities [37].

The applications of stimuli-responsive drug delivery systems span various medical fields, particularly in oncology, immunotherapy, and chronic diseases management. Cancer therapy has been a major area of research and application for SRDDS due to the need for precise delivery to tumor tissues while minimizing effects on healthy cells. For instance, pH-sensitive nanoparticles can selectively release chemotherapeutic agents in the acidic microenvironment typical of many tumors, which not only enhances the drug concentration at the tumor site but also reduces systemic toxicity [37].

In immunotherapy, SRDDS can facilitate the targeted delivery of immunemodulating agents to tumor sites, promoting a more robust immune response. Recent studies have shown that biodegradable nanoparticles engineered to degrade in response to specific tumor markers can increase the therapeutic efficacy of checkpoint inhibitors and other novel immunotherapeutics.

Chronic diseases such as diabetes also benefit from this technology. For example, glucose-sensitive insulin delivery systems have been developed, which release insulin in response to rising blood glucose levels, offering a potential solution for better glycemic control in diabetic patients. Such systems could significantly enhance patient compliance and quality of life by minimizing the need for manual monitoring and administration of insulin [38].

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Furthermore, SRDDS have found utility in the field of gene therapy, delivering nucleic acids in response to specific intracellular signals, thereby improving the efficiency and safety of gene delivery processes. Advances in this domain also include the use of stimuli-responsive materials to design systems capable of overcoming biological barriers, such as the blood-brain barrier, highlighting their potential for treating neurological disorders [38].

While SRDDS hold immense promise, several challenges remain before these systems can be fully realized in clinical settings. Issues such as scalability in manufacturing, the complexity of human biological responses, and regulatory hurdles must be addressed. Moreover, the long-term stability and biocompatibility of these advanced materials need to be thoroughly evaluated through comprehensive preclinical and clinical studies [39].

Interdisciplinary collaboration among chemists, biologists, pharmacologists, and engineers will be crucial in overcoming these obstacles. Continuous research and innovation in polymer chemistry, nanotechnology, and bioinformatics will foster the development of next-generation stimuli-responsive systems that are safe, effective, and versatile [40].

Nanotechnology for RNA-based Therapeutics: Challenges and Opportunities:

The emergence of RNA-based therapeutics represents a groundbreaking paradigm in modern medicine, offering novel strategies for the treatment of a spectrum of diseases, including cancer, viral infections, and genetic disorders. The potential of these therapies is significantly augmented through the integration of nanotechnology, which provides innovative solutions for delivery, stability, and efficacy of RNA molecules. This essay explores the myriad opportunities that nanotechnology presents for RNA-based therapeutics, while also addressing the associated challenges that must be navigated to fully realize their clinical potential [40].

RNA therapeutics encompass a diverse range of therapeutic modalities, including small interfering RNA (siRNA), messenger RNA (mRNA), and antisense oligonucleotides (ASOs). These molecules can modulate gene expression in a targeted manner, offering the potential to correct or silence genes implicated in various diseases. In comparison to traditional small molecule drugs, RNA-based therapies provide greater specificity and reduced off-target effects, making them particularly appealing in the realm of precision medicine. However, despite their promise, several hurdles remain, particularly in terms of delivery mechanisms [41].

The Role of Nanotechnology in RNA Delivery

One of the primary limitations of RNA-based therapeutics is their susceptibility to rapid degradation by nucleases in biological fluids and their difficulty in crossing cellular membranes. This is where nanotechnology plays a transformative role. Nanoparticles, which encompass a diverse range of materials such as lipids, polymers,

and inorganic substances, can be engineered to encapsulate RNA molecules, thereby enhancing their stability and regulating their release profiles [42].

1. Nanoparticle Design: The versatility of nanoparticle design allows for tailored properties that can improve the pharmacokinetics and biodistribution of RNA therapeutics. Lipid nanoparticles (LNPs), for instance, have been particularly successful in delivering mRNA vaccines, notably those developed for COVID-19. These LNPs facilitate cellular uptake, protect mRNA from degradation, and enable the translation of RNA into protein [42].

2. Targeting Mechanisms: The surface properties of nanoparticles can be modified to achieve targeted delivery through ligand-receptor interactions. By conjugating targeting moieties, such as antibodies or peptides, nanoparticles can preferentially deliver RNA therapeutics to specific cell types or tissues, minimizing off-target effects and enhancing therapeutic efficacy [43].

3. Controlled Release: Nanotechnology also enables controlled release of RNA therapeutics. For instance, encapsulation in biodegradable polymers can allow for a sustained release of RNA molecules over time, providing prolonged therapeutic action and reducing the frequency of administration.

Challenges in the Integration of Nanotechnology and RNA Therapeutics

While the integration of nanotechnology into RNA-based therapeutics presents monumental opportunities, several challenges must be addressed to facilitate their successful translation into clinical practice.

1. Manufacturing and Scalability: The production of RNA therapeutics and their nanocarriers must meet stringent regulatory standards, often posing significant challenges in terms of scalability and reproducibility. The manufacturing processes for nanoparticles need to be well-defined in order to ensure consistent quality and therapeutic efficacy across different batches [43].

2. Safety and Biocompatibility: The safety profile of nanoparticles is a critical consideration. Some materials used in nanoparticle formulation may elicit immune responses or other adverse effects. Understanding the biocompatibility of nanoparticles is essential to mitigate risks and ensure patient safety, especially for prolonged treatments [44].

3. Regulatory Hurdles: Navigating the regulatory landscape for newly developed RNA-based therapies and their nanosystems can be complex and timeconsuming. Regulatory bodies require comprehensive data on the pharmacodynamics, pharmacokinetics, and long-term effects of these therapies, leading to additional delay in their advancement to clinical use [44].

4. Stability and Storage: RNA therapeutics are inherently unstable and require stringent storage conditions to maintain their functionality. Developing nanoparticles that can stabilize RNA molecules while allowing for simple handling and transport is a challenge that necessitates innovative solutions [45].

Future Directions and Opportunities

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Almansour, Mohammad Marzouq Alfalakah, Saeed Mana Rukban Almansuor, Hadi Ahmed Mohammed
Alyami, Mohammed Sulaiman Awadh Al Makir, Madhi Huwayj Alsallum, Hassan Saeed Al Mansour, Ali Hadi
Maien Alsulayi, Alhamzah Abbas Ahmed Almakrami

Despite the challenges, the intersection of nanotechnology and RNA-based therapeutics offers exciting opportunities for advancing medical treatment. Several potential avenues warrant attention:

1.   Personalized Medicine: Nanotechnology can be harnessed to produce customized RNA therapeutics tailored to individual patient profiles, enabling more precise and effective treatments. This could lead to significant strides in the management of complex diseases where traditional therapies have failed [46].

2.   Combination Therapies: Utilizing nanotechnology to deliver RNA therapeutics in conjunction with other modalities, such as conventional chemotherapy or immunotherapy, could enhance overall efficacy and overcome drug resistance [47].

3.   Smart Delivery Systems: The development of "smart" nanoparticles that respond to specific physiological stimuli (e.g., pH, temperature, or specific enzymes) can lead to improved therapeutic outcomes. These systems can release RNA therapeutics in response to specific disease states, further enhancing the precision of treatment [48].

4.   Enhanced Diagnostic Capabilities: Nanotechnology can also play a significant role in the development of diagnostics that utilize RNA, further enabling the monitoring of disease progression and therapy response, and thereby tailoring treatment approaches in real-time [49].

Regulatory and Safety Considerations in Nanomedicine:

Nanomedicine, the application of nanotechnology in the field of medicine, represents a revolutionary frontier in healthcare. It involves the utilization of nanoparticles and nanoscale materials for diagnosis, treatment, and prevention of disease at a molecular level. Given its vast potential, nanomedicine offers unprecedented opportunities for targeted drug delivery, enhanced imaging techniques, and advanced therapeutic systems. Nevertheless, the unique properties of nanomaterials necessitate thorough regulatory oversight and comprehensive safety evaluations to address the associated risks, ensuring that innovations do not outpace safety measures [50].

Nanomedicine encompasses a wide variety of applications, including but not limited to drug delivery systems, imaging agents, and tissue engineering. Materials ranging from liposomes to dendrimers are engineered at the nanoscale, taking advantage of their size to modify drug absorption, distribution, metabolism, and excretion mechanisms. The ability to transport therapeutics precisely to target sites—such as malignant tumors—has given rise to the concept of personalized medicine, tailored to meet the specific needs of individual patients. However, while the promise of nanomedicine is robust, it introduces a range of complexities that require rigorous regulatory frameworks and safety assessments [51].

Regulating nanomedicine presents unique challenges that traditional regulatory approaches may not adequately address. Current regulatory bodies such as the U.S.

Food and Drug Administration (FDA), the European Medicines Agency (EMA), and other global health agencies are continually adapting their guidelines to keep pace with advancements in nanotechnology. At the core of these regulatory processes is the need for a robust scientific understanding of nanomaterials, including their behavior, interactions within biological systems, and potential long-term effects [52].

A significant challenge in regulation is the categorization of nanomaterials. Depending on their size, shape, surface properties, and chemical composition, nanomaterials can exhibit distinct biological interactions compared to their macrosized counterparts. Regulatory agencies are increasingly recognizing the necessity to develop specific guidelines for the evaluation of nanomedicines, considering aspects like particle characterization, safety assessments, pharmacokinetics, and toxicity studies [53].

In the United States, the FDA established the Nanotechnology Task Force to provide a unified approach to the assessment and regulation of nanotechnology applications. Their guiding principles emphasize the importance of scientific rigor in evaluating the safety of nanomedicine products while also maintaining a balance between innovation and regulatory oversight. The FDA's approach includes preclinical assessments, clinical trial protocols, and post-market surveillance to ensure that the benefits of nanomedicine extend beyond theoretical applications [54].

The EMA has similarly produced guidance documents focusing on the development of nanomedicines, addressing key aspects such as production and characterization, safety evaluation, and efficacy assessments. These guidelines emphasize a case-bycase approach to evaluating nanomedicine products, acknowledging the importance of specialized data categories that consider the unique properties of nanomaterials [54].

Safety considerations in nanomedicine encompass a broad spectrum of issues. Primarily, the potential toxicity of nanoparticles must be thoroughly assessed, as their small size allows them to infiltrate cellular structures and biological systems in ways that larger particles cannot. The biocompatibility of nanomaterials is paramount; materials must not provoke adverse immune responses and should be easily metabolized or excreted without accumulating in body tissues [55].

In vitro and in vivo studies are crucial components of safety assessments for nanomedicine. Researchers conduct extensive toxicology studies to evaluate the effects of nanoparticles on cellular functions, organ systems, and overall biological pathways. Importantly, the behavior of nanoparticles can vary significantly based on their size, shape, surface charge, and coating, which means that safety data collected for one type of nanoparticle may not be applicable to another, even if they share similar chemical compositions [56].

Another area of concern is the potential for unintended environmental impacts, particularly with the increasing use of nanomaterials in consumer products ranging from cosmetics to food packaging. Regulatory bodies are developing frameworks to address the lifecycle of nanomaterials—from production to disposal—ensuring that environmental safety remains a priority alongside human health considerations [56].

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The unique nature of nanomedicine also raises ethical considerations, particularly regarding consent and the public's understanding of nanoscale technologies. Patient education becomes vital, as individuals must be informed about the implications of novel treatments, including potential risks and uncertainties associated with nanomedicine. Furthermore, public trust is integral to the adoption of these new technologies; therefore, transparency in regulatory processes and safety assessments is essential [57].

The dissemination of accurate information regarding nanomedicine is crucial to mitigate fear and misunderstanding among the general public. Engaging stakeholders—including patients, healthcare providers, and regulatory bodies—is necessary to ensure that safety concerns are appropriately addressed while fostering an environment conducive to innovation [58].

Future Perspectives: Integrating AI and Personalized Medicine in Nanotechnology:

The convergence of artificial intelligence (AI), personalized medicine, and nanotechnology represents a transformative frontier in healthcare. As we stand on the cusp of profound advancements, these fields not only offer the potential to enhance therapeutic efficacy but also promise to revolutionize how we approach disease prevention, diagnosis, and treatment. This essay explores the integration of AI and personalized medicine within the realm of nanotechnology, addressing current innovations, potential applications, and future directions [58].

Understanding the Core Components

To comprehend the implications of integrating AI with personalized medicine and nanotechnology, it is crucial to define each component succinctly.

Nanotechnology refers to the manipulation of matter on an atomic or molecular scale, typically at dimensions less than 100 nanometers. This field has yielded a plethora of applications in medicine, including drug delivery systems, diagnostic tools, and imaging agents that enhance the detection and treatment of diseases [59].

Personalized medicine, also known as precision medicine, emphasizes tailoring medical treatment to the individual characteristics of each patient. By leveraging genetic, environmental, and lifestyle factors, personalized medicine aims to optimize therapeutic outcomes and minimize adverse effects [59].

Artificial intelligence, particularly in the form of machine learning and deep learning, incorporates computational algorithms that can analyze vast datasets, recognize patterns, and make predictions. AI has emerged as a powerful tool in numerous domains, facilitating enhanced decision-making, automating tasks, and uncovering insights hidden within complex biological data [60].

Current Innovations and Applications

The integration of AI with personalized medicine and nanotechnology is not merely theoretical; it is already manifesting in various forms. One of the most significant

applications is in drug delivery systems. Nanoparticles designed to carry specific drugs can be engineered to respond to AI-driven analysis of individual patient profiles. By assessing a patient's unique biological markers via AI algorithms, nanoparticles can be programmed to release their payload in a targeted manner, thus optimizing the therapeutic response while minimizing side effects [60].

In the realm of diagnostics, the incorporation of AI into nanotechnology has led to the development of advanced biosensors. These sensors utilize nanoscale materials that can detect biomarkers associated with particular diseases. Coupled with machine learning algorithms, these devices can interpret complex data patterns, facilitate early diagnosis, and provide real-time monitoring. For example, AI-enabled nanodiagnostics can significantly improve cancer detection rates by analyzing blood samples for circulating tumor DNA, which may lead to personalized and timely interventions [61].

AI's impact is particularly evident in the drug development process. Traditional methods are often lengthy and plagued by high failure rates. By integrating AI with nanotechnology, researchers can simulate drug interactions at the molecular level, identify potential candidates faster, and optimize formulations for better efficacy and safety. Nanomedicine combined with predictive AI models enables a more streamlined approach to understanding how drugs behave in the body, which could drastically reduce the time and cost of bringing new therapies to market [61].

Moreover, AI can enhance clinical trial design. Personalized medicine efforts benefit from AI's ability to analyze large datasets derived from genetic studies and clinical outcomes. By utilizing this data, researchers can identify optimal subject populations, stratify participants based on genetic profiles, and even predict which individuals are more likely to respond to a particular treatment. This data-driven approach not only increases the likelihood of trial success but also ensures that patients receive the most appropriate therapies tailored to their genetic makeup [62].

While the integration of AI, personalized medicine, and nanotechnology holds immense promise, it is imperative to address the ethical and accessibility issues that arise from these advancements. One of the foremost concerns is data privacy. The reliance on AI requires vast amounts of patient data, raising questions about confidentiality, informed consent, and the potential for misuse [63].

Furthermore, as personalized medicine relies heavily on genetic information, there is a risk of exacerbating existing health disparities. Ensuring that these technologies are accessible to all populations, especially marginalized communities, is crucial. Policymakers will need to implement frameworks that promote equitable access to innovative treatments and safeguard against discrimination, particularly in genetic testing and personalized therapies [64].

The future of integrating AI, personalized medicine, and nanotechnology in healthcare is brimming with potential. Advances in genomics and biotechnology will pave the way for even more nuanced understandings of diseases and their mechanisms. As these technologies mature, their integration will likely lead to the emergence of smart therapeutic platforms capable of real-time adjustments based on patient responses [64].

Saeed Saleh Mohammed Almansour, Yahya Mohammed Abdullah Almasaabi, Nasser Saleh Mohammed Almansour, Mohammad Marzouq Alfalakah, Saeed Mana Rukban Almansuor, Hadi Ahmed Mohammed Alyami, Mohammed Sulaiman Awadh Al Makir, Madhi Huwayj Alsallum, Hassan Saeed Al Mansour, Ali Hadi Maien Alsulayi, Alhamzah Abbas Ahmed Almakrami

Moreover, the integration of AI with wearable nanodevices could lead to the development of personalized health monitoring systems. These devices could continuously assess physiological parameters and adapt treatments accordingly, ushering in an era of proactivity in healthcare rather than reactivity [65].

In addition, the ongoing research in nanomaterials and their applications in drug delivery will continue to evolve. The ability to design nanoparticles that can navigate biological barriers and deliver drugs to specific tissues or cells will be paramount [66].

2. Conclusion:

In conclusion, nanotechnology represents a significant advancement in drug delivery systems, offering innovative solutions to longstanding challenges in pharmacotherapy. The ability to design and engineer nanoparticles and other nanocarriers has revolutionized the way drugs are formulated and delivered, enhancing their bioavailability, efficacy, and safety profiles. Current trends highlight the growing importance of targeted delivery mechanisms, which allow for precise treatment of diseases such as cancer, while minimizing adverse effects on healthy tissues. Additionally, the development of stimuli-responsive systems and the integration of nanotechnology with cutting-edge therapies, such as RNA-based treatments, open new avenues for personalized medicine. Looking to the future, the potential of nanotechnology in drug delivery is immense, driven by ongoing research and technological advancements. However, addressing regulatory challenges and safety concerns will be crucial for the successful translation of these innovations into clinical practice. As we move forward, the collaboration between researchers, clinicians, and regulatory bodies will be essential to harness the full potential of nanotechnology, ultimately leading to more effective and tailored therapeutic strategies that improve patient outcomes and quality of life.

References

Mohanty SK, Swamy MK, Sinniah UR, Anuradha M. Leptadenia reticulata (Retz.) Wight & Arn. (Jivanti): botanical, agronomical, phytochemical, pharmacological, and biotechnological aspects. Molecules. 2017;22. doi: 10.3390/molecules22061019.

Beutler JA. Natural products as a foundation for drug discovery. Curr Prot Pharmacol. 2009;46(1):9–11. doi: 10.1002/0471141755.ph0911s46.

Thilakarathna SH, Rupasinghe H. Flavonoid bioavailability and attempts for bioavailability enhancement. Nutrients. 2013;5:3367–3387. doi: 10.3390/nu5093367.

Haba Y, Kojima C, Harada A, Ura T, Horinaka H, Kono K. Preparation of poly (ethylene glycol)-modified poly (amido amine) dendrimers encapsulating gold nanoparticles and their heat-generating ability. Langmuir. 2007;23:5243–5246. doi: 10.1021/la0700826.

Siddiqui AA, Iram F, Siddiqui S, Sahu K. Role of natural products in drug discovery process. Int J Drug Dev Res. 2014;6(2):172–204.

Watkins R, Wu L, Zhang C, Davis RM, Xu B. Natural product-based nanomedicine: recent advances and issues. Int J Nanomed. 2015;10:6055. doi: 10.2147/IJN.S92162.

Arayne MS, Sultana N, Qureshi F. Nanoparticles in delivery of cardiovascular drugs. Pak J Pharm Sci. 2007;20:340–348.

Rodrigues T, Reker D, Schneider P, Schneider G. Counting on natural products for drug design. Nat Chem. 2016;8:531. doi: 10.1038/nchem.2479.

Martinho N, Damgé C, Reis CP. Recent advances in drug delivery systems. J Biomater Nanobiotechnol. 2011;2:510. doi: 10.4236/jbnb.2011.225062.

Lam P-L, Wong W-Y, Bian Z, Chui C-H, Gambari R. Recent advances in green nanoparticulate systems for drug delivery: efficient delivery and safety concern. Nanomedicine. 2017;12:357–385. doi: 10.2217/nnm-2016-0305.

Rudramurthy GR, Swamy MK, Sinniah UR, Ghasemzadeh A. Nanoparticles: alternatives against drug-resistant pathogenic microbes. Molecules. 2016;21:836. doi: 10.3390/molecules21070836.

Mirza AZ, Siddiqui FA. Nanomedicine and drug delivery: a mini review. Int Nano Lett. 2014;4:94. doi: 10.1007/s40089-014-0094-7.

Bonifácio BV, da Silva PB, dos Santos Ramos MA, Negri KMS, Bauab TM, Chorilli M. Nanotechnology-based drug delivery systems and herbal medicines: a review. Int J Nanomed. 2014;9:1. doi: 10.2217/nnm.13.186.

Liu Z, Tabakman S, Welsher K, Dai H. Carbon nanotubes in biology and medicine: in vitro and in vivo detection, imaging and drug delivery. Nano Res. 2009;2:85–120. doi: 10.1007/s12274-009-9009-8.

Jahangirian H, Lemraski EG, Webster TJ, Rafiee-Moghaddam R, Abdollahi Y. A review of drug delivery systems based on nanotechnology and green chemistry: green nanomedicine. Int J Nanomed. 2017;12:2957. doi: 10.2147/IJN.S127683.

Orive G, Gascon AR, Hernández RM, Domínguez-Gil A, Pedraz JL. Techniques: new approaches to the delivery of biopharmaceuticals. Trends Pharmacol Sci. 2004;25:382–387. doi: 10.1016/j.tips.2004.05.006.

Razzacki SZ, Thwar PK, Yang M, Ugaz VM, Burns MA. Integrated microsystems for controlled drug delivery. Adv Drug Deliv Rev. 2004;56:185–198. doi: 10.1016/j.addr.2003.08.012.

Joseph RR, Venkatraman SS. Drug delivery to the eye: what benefits do nanocarriers offer? Nanomedicine. 2017;12:683–702. doi: 10.2217/nnm-2016-0379.

Swamy MK, Sinniah UR. Patchouli (Pogostemon cablin Benth.): botany, agrotechnology and biotechnological aspects. Ind Crops Prod. 2016;87:161–176. doi: 10.1016/j.indcrop.2016.04.032.

Martinho N, Damgé C, Reis CP. Recent advances in drug delivery systems. J Biomater Nanobiotechnol. 2011;2:510. doi: 10.4236/jbnb.2011.225062.

Attia M. F., Anton N., Wallyn J., Omran Z., Vandamme T. F. (2019). An overview of active and passive targeting strategies to improve the nanocarriers efficiency to tumour sites. J. Pharm. Pharmacol. 71, 1185–1198.

Alhakamy N. A., Fahmy U. A., Eldin S. M. B., Ahmed O. A. A., Aldawsari H. M., Okbazghi S. Z., et al. (2022). Scorpion venom-functionalized quercetin phytosomes for breast cancer management: in vitro response surface optimization and anticancer activity against MCF-7 cells. POLYMERS 14, 93.

Almoustafa H. A., Alshawsh M. A., Chik Z. (2021). Targeted polymeric nanoparticle for anthracycline delivery in hypoxia-induced drug resistance in metastatic breast cancer cells. ANTI-CANCER DRUGS 32, 745–754.

Ahuja A., Narde G. K., Wadi N. M. A., Meenakshi D. U. (2021). Drug targeting approaches and use of drug delivery systems in management of cancer. Curr. Pharm. Des. 27, 4593–4609.

Saeed Saleh Mohammed Almansour, Yahya Mohammed Abdullah Almasaabi, Nasser Saleh Mohammed Almansour, Mohammad Marzouq Alfalakah, Saeed Mana Rukban Almansuor, Hadi Ahmed Mohammed Alyami, Mohammed Sulaiman Awadh Al Makir, Madhi Huwayj Alsallum, Hassan Saeed Al Mansour, Ali Hadi Maien Alsulayi, Alhamzah Abbas Ahmed Almakrami

Alimoradi H., Greish K., Barzegar-Fallah A., Alshaibani L., Pittala V. (2018). Nitric oxidereleasing nanoparticles improve doxorubicin anticancer activity. Int. J. NANOMEDICINE 13, 7771–7787.

Abumanhal-Masarweh H., Koren L., Zinger A., Yaari Z., Krinsky N., Kaneti G., et al. (2019). Sodium bicarbonate nanoparticles modulate the tumor pH and enhance the cellular uptake of doxorubicin. J. Control. RELEASE 296, 1–13.

Bray F., Ferlay J., Soerjomataram I., Siegel R. L., Torre L. A., Jemal A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J. Clin. 68, 394–424.

Bilan R., Nabiev I., Sukhanova A. (2016). Quantum dot-based nanotools for bioimaging, diagnostics, and drug delivery. Chembiochem 17, 2103–2114.

Boix-Montesinos P., Soriano-Teruel P. M., Armiñán A., Orzáez M., Vicent M. J. (2021). The past, present, and future of breast cancer models for nanomedicine development. Adv. Drug Deliv. Rev. 173, 306–330.

Anselmo A. C., Mitragotri S. (2015). A review of clinical translation of inorganic nanoparticles. Aaps J. 17, 1041–1054.

Al-Humaidi R. B., Fayed B., Sharif S. I., Noreddin A., Soliman S. S. M. (2021). Role of exosomes in breast cancer management: evidence-based review. Curr. Cancer Drug Targets 21, 666–675.

Blanco E., Shen H., Ferrari M. (2015). Principles of nanoparticle design for overcoming biological barriers to drug delivery. Nat. Biotechnol. 33, 941–951.

Barenholz Y. (2012). Doxil®--the first FDA-approved nano-drug: lessons learned. J. Control Release 160, 117–134.

Aniogo E. C., Adimuriyil George Plackal B., Abrahamse H. (2019). The role of photodynamic therapy on multidrug resistant breast cancer. Cancer Cell. Int. 19, 91.

Bertrand N., Grenier P., Mahmoudi M., Lima E. M., Appel E. A., Dormont F., et al. (2017). Mechanistic understanding of in vivo protein corona formation on polymeric nanoparticles and impact on pharmacokinetics. Nat. Commun. 8, 777.

Blum J. L., Flynn P. J., Yothers G., Asmar L., Geyer C. E., Jr., Jacobs S. A., et al. (2017). Anthracyclines in early breast cancer: the ABC trials-USOR 06-090, NSABP B-46I/USOR 07132, and NSABP B-49 (NRG oncology). J. Clin. Oncol. 35, 2647–2655.

Aria M., Cuccurullo C. (2017). bibliometrix: an R-tool for comprehensive science mapping analysis. J. Inf. 11, 959–975.

Bonadonna G., Brusamolino E., Valagussa P., Rossi A., Brugnatelli L., Brambilla C., et al. (1976). Combination chemotherapy as an adjuvant treatment in operable breast cancer. N. Engl. J. Med. 294, 405–410.

Bowman K. M., Kumthekar P. (2018). Medical management of brain metastases and leptomeningeal disease in patients with breast carcinoma. Future Oncol. 14, 391–407.

Zhang L, Wang Y, Yang D, Huang W, Hao P, Feng S, Appelhans D, Zhang T, Zan X. Shape effect of nanoparticles on tumor penetration in monolayers versus spheroids. Mol Pharm. 2019;16:2902–2911.

Ghaffar KA, Marasini N, Giddam AK, Batzloff MR, Good MF, Skwarczynski M, Toth I. The role of size in development of mucosal liposome-lipopeptide vaccine candidates against group A streptococcus. Med Chem. 2016;13:22–27.

Black KC, Wang Y, Luehmann HP, Cai X, Xing W, Pang B, Zhao Y, Cutler CS, Wang LV, Liu Y, Xia Y. Radioactive 198Au-doped nanostructures with different shapes for in vivo analyses of their biodistribution, tumor uptake, and intratumoral distribution. ACS Nano. 2014;8:4385–4394.

Donaldson K, Tran L, Jimenez LA, Duffin R, Newby DE, Mills N, MacNee W, Stone V. Combustion-derived nanoparticles: A review of their toxicology following inhalation exposure. Part Fibre Toxicol. 2005;2:10.

Murugan K, Choonara YE, Kumar P, Bijukumar D, du Toit LC, Pillay V. Parameters and characteristics governing cellular internalization and trans-barrier trafficking of nanostructures. Int J Nanomedicine. 2015;10:2191–2206.

Newman SP. Delivering drugs to the lungs: The history of repurposing in the treatment of respiratory diseases. Adv Drug Deliv Rev. 2018;133:5–18.

Jeong J, Lee S, Kim SH, Han Y, Lee DK, Yang JY, Jeong J, Roh C, Huh YS, Cho WS. Evaluation of the dose metric for acute lung inflammogenicity of fast-dissolving metal oxide nanoparticles. Nanotoxicology. 2016;10:1448–1457.

Gratton SE, Ropp PA, Pohlhaus PD, Luft JC, Madden VJ, Napier ME, DeSimone JM. The effect of particle design on cellular internalization pathways. Proc Natl Acad Sci USA. 2008;105:11613–11618.

Murgia X, Pawelzyk P, Schaefer UF, Wagner C, Willenbacher N, Lehr CM. Size-limited penetration of nanoparticles into porcine respiratory mucus after aerosol deposition. Biomacromolecules. 2016;17:1536–1542.

Pison U, Welte T, Giersig M, Groneberg DA. Nanomedicine for respiratory diseases. Eur J Pharmacol. 2006;533:341–350.

Poh TY, Mohamed Ali NAB, Aogáin MM, Kathawala MH, Setyawati MI, Ng KW, Chotirmall SH. Inhaled nanomaterials and the respiratory microbiome: Clinical, immunological and toxicological perspectives. Part Fibre Toxicol. 2018;15:46.

Auria-Soro C, Nesma T, Juanes-Velasco P, Landeira-Viñuela A, Fidalgo-Gomez H, AcebesFernandez V, Gongora R, Parra MJA, Manzano-Roman R, Fuentes M. Interactions of nanoparticles and biosystems: Microenvironment of nanoparticles and biomolecules in nanomedicine. Nanomaterials (Basel). 2019;9:1365.

Fröhlich E, Salar-Behzadi S. Toxicological assessment of inhaled nanoparticles: Role of in vivo, ex vivo, in vitro, and in silico studies. Int J Mol Sci. 2014;15:4795–4822.

Lin X, Zuo YY, Gu N. Shape affects the interactions of nanoparticles with pulmonary surfactant. Sci China Mater. 2015;58:28–37.

Bakand S, Hayes A, Dechsakulthorn F. Nanoparticles: A review of particle toxicology following inhalation exposure. Inhal Toxicol. 2012;24:125–135.

Wang N, Feng Y. Elaborating the role of natural products-induced autophagy in cancer treatment: achievements and artifacts in the state of the art. BioMed Res Int. 2015;2015:934207.

Holzinger M, Le Goff A, Cosnier S. Nanomaterials for biosensing applications: a review. Front Chem. 2014;2:63.

McNamara K, Tofail SA. Nanosystems: the use of nanoalloys, metallic, bimetallic, and magnetic nanoparticles in biomedical applications. Phys Chem Chem Phys. 2015;17:27981–27995.

Kabanov AV, Lemieux P, Vinogradov S, Alakhov V. Pluronic® block copolymers: novel functional molecules for gene therapy. Adv Drug Deliv Rev. 2002;54:223–233.

Sanna V, Roggio AM, Siliani S, Piccinini M, Marceddu S, Mariani A, Sechi M. Development of novel cationic chitosan-and anionic alginate–coated poly (d, l-lactide-co-glycolide) nanoparticles for controlled release and light protection of resveratrol. Int J Nanomed. 2012;7:5501.

De Jong WH, Borm PJ. Drug delivery and nanoparticles: applications and hazards. Int J Nanomed. 2008;3:133.

Obeid MA, Al Qaraghuli MM, Alsaadi M, Alzahrani AR, Niwasabutra K, Ferro VA. Delivering natural products and biotherapeutics to improve drug efficacy. Ther Deliv. 2017;8:947–956.

Saeed Saleh Mohammed Almansour, Yahya Mohammed Abdullah Almasaabi, Nasser Saleh Mohammed Almansour, Mohammad Marzouq Alfalakah, Saeed Mana Rukban Almansuor, Hadi Ahmed Mohammed Alyami, Mohammed Sulaiman Awadh Al Makir, Madhi Huwayj Alsallum, Hassan Saeed Al Mansour, Ali Hadi Maien Alsulayi, Alhamzah Abbas Ahmed Almakrami

Tan Q, Liu W, Guo C, Zhai G. Preparation and evaluation of quercetin-loaded lecithinchitosan nanoparticles for topical delivery. Int J Nanomed. 2011;6:1621.

Ouattara B, Simard RE, Holley RA. Piette GJ-P, Bégin A: Antibacterial activity of selected fatty acids and essential oils against six meat spoilage organisms. Int J Food Microbiol. 1997;37:155–162.

Abdelwahab SI, Sheikh BY, Taha MME, How CW, Abdullah R, Yagoub U, El-Sunousi R, Eid EE. Thymoquinone-loaded nanostructured lipid carriers: preparation, gastroprotection, in vitro toxicity, and pharmacokinetic properties after extravascular administration. Int J Nanomed. 2013;8:2163.

Golovin YI, Gribanovsky SL, Golovin DY, Klyachko NL, Majouga AG, Master AM, Sokolsky M, Kabanov AV. Towards nanomedicines of the future: remote magnetomechanical actuation of nanomedicines by alternating magnetic fields. J Control Release. 2015;219:43–60.

Sharma G, Raturi K, Dang S, Gupta S, Gabrani R. Combinatorial antimicrobial effect of curcumin with selected phytochemicals on Staphylococcus epidermidis. J Asian Nat Prod Res. 2014;16:535–541.