

RECENT ADVANCES IN DRUG DELIVERY SYSTEMS: FOCUS ON NANOFORMULATIONS AND CONTROLLED RELEASE

Priya Khandagale

Department of Bioinformatics,
MGM Institute of Bioscience &
Technology, Aurangabad,
Maharashtra, India.,

Correspondence:

Ms. Priya Khandagale,
Department of Bioinformatics,
MGM Institute of Bioscience &
Technology, Aurangabad,
Maharashtra, India.

Email:
priyakhandagalenov@gmail.com

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ABSTRACT

Recent advancements in drug delivery systems (DDS) have revolutionized the treatment of various diseases by improving drug bioavailability, targeting, and therapeutic efficacy while minimizing side effects. Among these innovations, nano formulations and controlled release systems stand out for their ability to deliver drugs with precision and sustained release. Nano formulations, which include nanoparticles, liposomes, micelles, and dendrimers, offer unique properties such as enhanced stability, biocompatibility, and the ability to target specific cells or tissues. These advances enable the delivery of a wide range of therapeutic agents, including small molecules, proteins, peptides, and nucleic acids. Controlled release mechanisms, including diffusion-controlled, degradation-controlled, and stimuli-responsive systems, further enhance the therapeutic profile of drugs by maintaining optimal drug concentrations over extended periods, reducing the need for frequent dosing. However, challenges remain in scaling up production, addressing safety and toxicity concerns, and meeting regulatory requirements for clinical applications. This review highlights recent developments in nano formulations and controlled release systems, exploring their applications in cancer therapy, chronic diseases, gene delivery, and vaccines. The article also discusses emerging technologies, including personalized drug delivery and nanorobotics, and outlines future directions for further improving the efficacy and safety of DDS in clinical settings.

KEYWORDS: Nano formulations, Drug Delivery Systems, Controlled Release, Nanomedicine, Targeted Therapy

INTRODUCTION

Drug Delivery Systems (DDS) have evolved significantly over the years, primarily focusing on enhancing the efficacy and safety of therapeutic agents. Conventional DDS often face limitations such as poor bioavailability, rapid systemic clearance, and non-specific distribution, which can lead to increased side effects and reduced therapeutic outcomes. These challenges underscore the necessity for advanced drug delivery strategies that can improve the precision and control of drug administration in modern therapeutics. The integration of novel technologies, particularly nanotechnology, has emerged as a promising solution to address these limitations by enabling targeted delivery and enhanced release profiles.¹

The significance of nano formulations in drug delivery cannot be overstated. Nanotechnology facilitates the development of nanocarriers that can encapsulate therapeutic agents, allowing for

controlled and sustained release mechanisms. These nano formulations enhance the solubility and stability of drugs, improve their pharmacokinetic profiles, and enable targeted delivery to specific tissues or cells. Controlled release systems are particularly important as they can minimize peak plasma concentrations, thereby reducing toxicity while maintaining effective drug levels over extended periods. This approach is crucial in treating chronic conditions where consistent therapeutic levels are required. The objective of this review is to explore the advancements in drug delivery systems with a focus on nano formulations and controlled release mechanisms. This field, highlighting the innovative strategies employed to enhance drug delivery, aims to provide a comprehensive overview of the current state of research in delivery efficacy and safety. By examining various nanocarrier designs and their release kinetics, this review seeks to elucidate the potential of these advanced systems in improving therapeutic outcomes across different medical applications.²

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FUNDAMENTALS OF NANOMEDICINE

Nanotechnology represents a transformative approach in various fields, particularly in drug delivery systems (DDS). Defined by the manipulation of materials at the nanoscale (1-100 nanometres), nanomaterials exhibit unique physical and chemical properties that differ significantly from their bulk counterparts. These properties include a high surface area-to-volume ratio, enhanced reactivity, and the ability to interact with biological systems at the molecular level, making them ideal candidates for drug delivery applications. Various types of nanomaterials are utilized in this context, including nanoparticles, liposomes, dendrimers, and micelles. Each type offers distinct advantages: nanoparticles can improve solubility and bioavailability; liposomes provide biocompatibility and the ability to encapsulate both hydrophilic and hydrophobic drugs; dendrimers allow for precise drug loading and release; and micelles can solubilize poorly soluble drugs, enhancing their therapeutic efficacy.³

The mechanisms of nanoparticle-based drug delivery are influenced by several factors, including size and surface characteristics. The size of nanoparticles is critical; smaller particles can more easily penetrate biological barriers and accumulate in target tissues due to enhanced permeability and retention (EPR) effects. Surface characteristics, such as charge and hydrophilicity, also play a vital role in determining how nanoparticles interact with cells and biological fluids. Nanoparticles can be designed for passive targeting, where they exploit the leaky vasculature of tumors to accumulate at disease sites, or active targeting, which involves the conjugation of targeting ligands (e.g., antibodies or peptides) to the nanoparticle surface to enhance specificity towards particular cell types or tissues.

The benefits of nano formulations in drug delivery are substantial. They enhance bioavailability by improving solubility and stability of therapeutic agents, allowing for lower dosages and reduced frequency of administration. Targeted delivery reduces systemic side effects by concentrating the therapeutic effect at the desired site while sparing healthy tissues from exposure to high drug concentrations. Furthermore, nano formulations can facilitate controlled release mechanisms that prolong the therapeutic action of drugs, thereby enhancing patient compliance and overall treatment effectiveness. Collectively, these advantages position

nanomedicine as a promising frontier in modern therapeutics, paving the way for more effective and safer treatment options across various diseases.⁴

ADVANCES IN NANOFORMULATIONS FOR DRUG DELIVERY

Advancements in nano formulations for drug delivery have led to the development of a variety of new nanocarriers, including polymeric nanoparticles, liposomes, nanoemulsion, and micelles. Polymeric nanoparticles are particularly notable for their versatility and ability to encapsulate both hydrophilic and hydrophobic drugs, while liposomes offer biocompatibility and a capacity for sustained release. Nanoemulsion enhance the solubility of poorly soluble drugs, and micelles can effectively solubilize hydrophobic compounds. A significant focus in this area is on the use of biodegradable and biocompatible nanomaterials, which minimize toxicity and environmental impact post-administration. These materials are designed to degrade into non-toxic byproducts, thereby enhancing patient safety and reducing the risk of long-term accumulation in the body.

Functionalization and surface modification of nanocarriers are crucial strategies that enhance their stability and drug release profiles. Techniques such as covalent and non-covalent bonding allow for the attachment of various functional groups to the surfaces of nanoparticles, improving their interaction with biological systems. For instance, polyethylene glycol (PEG) is often used as a linker to increase solubility and reduce immunogenicity. Additionally, targeting strategies utilizing ligands and antibodies enable selective delivery to specific cells or tissues, enhancing therapeutic efficacy while minimizing side effects. This targeted approach is particularly beneficial in cancer therapy, where it is essential to deliver drugs directly to tumor cells while sparing healthy tissues.⁵

Different types of nano formulations cater to specific drug types, enhancing their therapeutic potential. For small molecule drugs, nanoparticles can improve solubility and bioavailability, allowing for lower dosages and reduced side effects. In the case of protein and peptide drugs, nano formulations protect these sensitive molecules from degradation, facilitating their delivery and maintaining efficacy. Furthermore, advancements in nanotechnology have enabled the effective delivery of nucleic acids such as siRNA and mRNA, which are critical for gene therapy

applications. These nano formulations can encapsulate nucleic acids within protective carriers that enhance cellular uptake and ensure controlled release at target sites⁴⁵. Overall, these advances in nano formulations represent a significant leap forward in drug delivery technology, promising improved outcomes in various therapeutic areas.⁶

CONTROLLED RELEASE DRUG DELIVERY SYSTEMS

Controlled release drug delivery systems (DDS) are designed to release therapeutic agents at predetermined rates, enhancing the efficacy and safety of treatments. The principles of controlled release involve various mechanisms such as diffusion-controlled, degradation-controlled, swelling-controlled, and osmosis-driven release. Diffusion-controlled release occurs when a drug is dispersed in a polymer matrix or encapsulated within a membrane, allowing it to diffuse through the barrier based on concentration gradients. Degradation-controlled release relies on the breakdown of the carrier material, which gradually releases the drug as it degrades over time. Swelling-controlled release involves the absorption of fluids by the polymer matrix, leading to an increase in volume and subsequent drug release. Lastly, osmosis-driven release utilizes osmotic pressure to facilitate drug expulsion from a semi-permeable membrane, typically maintaining a zero-order release profile as long as the concentration gradient is sustained.⁷

The advantages of controlled release systems are significant. They improve therapeutic efficacy by maintaining drug levels within a desired therapeutic range, which minimizes fluctuations that can lead to side effects. This approach also reduces toxicity by preventing peak concentrations that could cause adverse reactions. Additionally, controlled release systems enhance patient compliance by decreasing the frequency of dosing; patients are more likely to adhere to treatment regimens that require less frequent administration. Overall, these systems contribute to more effective and safer therapeutic outcomes.

Recent innovations in controlled release DDS include the development of smart and stimuli-responsive systems that react to specific environmental triggers such as pH or temperature changes. These systems can provide targeted and controlled drug delivery, enhancing therapeutic effects while minimizing side effects. Moreover, triggered release mechanisms utilizing external stimuli such as

magnetic fields, light exposure, or enzymatic activity allow for precise control over when and how much drug is released. These advancements represent a significant leap in drug delivery technology, offering tailored treatment options that can adapt to individual patient needs and specific disease states.⁸

CASE STUDIES AND APPLICATIONS OF NANOFORMULATIONS IN CONTROLLED RELEASE

Case studies and applications of nano formulations in controlled release have shown significant promise across various therapeutic areas, particularly in cancer therapy, chronic diseases, gene delivery, and vaccine development.

In drug delivery for cancer therapy, nano formulations have been pivotal in enhancing targeted treatment. For instance, liposomal formulations such as Doxil utilize liposomes to encapsulate doxorubicin, allowing for targeted delivery to tumor sites while minimizing systemic toxicity. Similarly, polymeric nanoparticles have been designed to release chemotherapeutic agents in a controlled manner, improving efficacy and reducing side effects by utilizing the enhanced permeability and retention (EPR) effect to accumulate at tumor sites. Studies have demonstrated that these formulations can significantly improve drug bioavailability and therapeutic outcomes in various cancers, including breast and lung cancer.

Nano formulations in chronic diseases such as diabetes, cardiovascular diseases, and neurological disorders also highlight their versatility. For diabetes management, nanoparticles can deliver insulin in a controlled manner, reducing the frequency of injections and improving glycemic control. In cardiovascular therapy, metal- and lipid-based nanoparticles have been employed to target atherosclerotic plaques, enhancing the delivery of cardioprotective agents while minimizing adverse effects. Moreover, in neurological disorders like Alzheimer's disease, nanoparticles facilitate the crossing of the blood-brain barrier (BBB), allowing for targeted delivery of therapeutic agents that can alleviate symptoms or slow disease progression.⁹

Advancements in gene and RNA-based drug delivery are also noteworthy. Recent innovations have focused on delivering small interfering RNA (siRNA), messenger RNA (mRNA), and CRISPR-based systems using

lipid nanoparticles or polymeric carriers. These nano formulations protect nucleic acids from degradation and enhance cellular uptake, allowing for effective gene silencing or editing. For example, lipid nanoparticles have been successfully used in mRNA vaccines for COVID-19, showcasing their ability to deliver genetic material effectively while ensuring controlled release.

In the realm of nanomedicine for vaccines, Nano formulations are increasingly being utilized to enhance vaccine efficacy through controlled release mechanisms. Nanoparticles can encapsulate antigens and adjuvants, providing sustained release that stimulates a more robust immune response over time. This approach not only improves the effectiveness of vaccines but also reduces the need for multiple doses. Recent studies have demonstrated that such formulations can enhance immune responses against various pathogens, including viruses and bacteria.

Overall, the integration of nano formulations into controlled release drug delivery systems presents a transformative approach across multiple therapeutic areas, offering improved efficacy, safety, and patient compliance.¹⁰

CHALLENGES AND LIMITATIONS

The challenges and limitations associated with nano formulations in drug delivery systems are multifaceted, encompassing scalability, safety, and regulatory issues.

Scalability and manufacturing challenges are significant barriers to the commercial production of nano formulations. The transition from laboratory-scale synthesis to industrial-scale manufacturing often encounters difficulties such as achieving uniformity in particle size, distribution, and shape. Common production methods include top-down approaches, which involve breaking down bulk materials into nanosized particles, and bottom-up techniques that build particles from molecular components. However, these methods can be energy-intensive and may lead to issues like aggregation and contamination during large-scale production. Additionally, the lack of well-defined optimization parameters complicates the reproducibility of nanoparticle characteristics, resulting in low yields and increased costs that hinder industrial acceptance of nano formulations.

Safety and toxicity concerns are paramount when considering the long-term effects of nanoparticles on human health and the environment. Although nanoparticles can enhance drug delivery efficacy, their

biocompatibility remains a critical issue. Studies have raised concerns about potential cytotoxicity, immunogenicity, and the accumulation of nanoparticles in tissues over time. The interaction of nanoparticles with biological systems can lead to unintended consequences, including oxidative stress and inflammatory responses. Thus, thorough evaluation of their long-term safety profiles is essential before they can be widely adopted in clinical applications.

Regulatory and ethical challenges further complicate the landscape for nano formulations. The regulatory framework governing nanomedicine is still evolving, with many countries lacking specific guidelines tailored to nanotechnology. This situation creates uncertainty regarding safety standards for clinical applications, as existing regulations may not adequately address the unique properties and behaviors of nanomaterials. As a result, navigating the regulatory landscape can be complex and time-consuming for developers seeking approval for new nano formulations. Moreover, ethical considerations surrounding the use of nanotechnology in medicine such as informed consent and equitable access must also be addressed to ensure responsible development and application of these advanced therapies.

In summary, while nano formulations hold great promise for enhancing drug delivery systems, significant challenges related to scalability, safety, and regulatory compliance must be overcome to realize their full potential in clinical practice.¹¹

FUTURE DIRECTIONS IN NANOFORMULATIONS AND CONTROLLED RELEASE

Future directions in nano formulations and controlled release systems are poised to leverage emerging technologies, personalized medicine, and innovative delivery mechanisms to enhance therapeutic efficacy and patient outcomes.

Emerging technologies such as artificial intelligence (AI) and machine learning are transforming the design and development of nanomedicines. AI can analyze vast datasets to identify patterns and optimize material properties, leading to the creation of more effective nano formulations tailored for specific therapeutic applications. For instance, AI algorithms can predict how different nanomaterials interact with biological systems, thereby facilitating the design of nanoparticles

that maximize drug delivery efficiency while minimizing toxicity. Additionally, the development of hybrid and multifunctional nanomaterials is gaining traction, where nanoparticles are engineered to perform multiple functions simultaneously such as delivering drugs while also providing diagnostic capabilities. This multifunctionality can significantly enhance treatment outcomes by allowing for real-time monitoring of therapeutic effects alongside drug delivery.

Personalized drug delivery is another promising direction in the field of nano formulations. Advances in genomics and patient-specific factors, such as genetic makeup and disease profiles, enable the tailoring of drug delivery systems (DDS) to individual patients. This approach aims to optimize therapeutic regimens by considering variations in metabolism, drug response, and disease characteristics among patients. By customizing nano formulations based on these factors, healthcare providers can improve treatment efficacy and reduce adverse effects, ultimately leading to better patient compliance and outcomes.

The integration of nanorobotics and smart drug delivery systems represents a cutting-edge frontier in nanomedicine. Future prospects include the development of autonomous drug delivery systems capable of responding to specific physiological conditions or stimuli. For example, nanorobots could be designed to navigate through the body and deliver drugs precisely where needed, triggered by environmental factors such as pH changes or specific biomolecules found in diseased tissues. This level of precision could revolutionize treatment strategies for complex diseases by ensuring that therapeutic agents are released only when and where they are most effective.

In summary, the future of nano formulations in controlled release systems is marked by the integration of advanced technologies like AI, personalized approaches tailored to individual patient needs, and innovative smart delivery mechanisms that promise to enhance the efficacy and safety of therapeutic interventions across various medical fields.¹²

CONCLUSION

In conclusion, recent advances in nano formulations and controlled release systems have significantly enhanced drug delivery, offering improved targeting, efficacy, and reduced side effects. These innovations are particularly impactful in treating cancer, chronic diseases, and gene-based therapies. Despite challenges in scalability, safety, and regulatory approval, the future of drug delivery looks promising with emerging technologies like personalized medicine and nanorobotics. Continued research and development will further optimize these systems, transforming therapeutic strategies and patient outcomes.

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