Nano-bio Hybrid Systems: a New Frontier in Targeted and Personalized Medicine

Snehal Dasharath Pawar[1*], Dhanasekar Jayakumar[2], Lathamani Lakshmanan[3], Selvakumar Muruganantham[4]

[1]Department of Pharmaceutics, Vivekanandha Pharmacy College, Veerachipalayam, Sankari, Salem, Tamil Nadu, India - 637 303.

[2]Department of Pharmaceutics, Vivekanandha Pharmacy College, Veerachipalayam, Sankari, Salem, Tamil Nadu, India - 637 303.

[3]Department of Pharmaceutics, Vivekanandha Pharmacy College, Veerachipalayam, Sankari, Salem, Tamil Nadu, India - 637 303.

[4]Department of Pharmaceutics, Vivekanandha Pharmacy College, Veerachipalayam, Sankari, Salem, Tamil Nadu, India - 637 303.

Corresponding author: sonudasratpawar@gmail.com

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Abstract:

The advancement of drug delivery systems has significantly improved therapeutic outcomes; however, conventional approaches continue to face limitations such as poor bioavailability, non-specific targeting, and systemic toxicity. Nanotechnology has emerged as a powerful tool to overcome these challenges by enabling controlled and targeted drug delivery. Among recent innovations, nano-bio hybrid systems have gained considerable attention due to their ability to integrate synthetic nanomaterials with biological components, thereby enhancing therapeutic efficiency and biocompatibility. The objective of this review is to provide a comprehensive overview of nano-bio hybrid systems and their role in targeted and personalized medicine. The article discusses various types of hybrid systems, preparation techniques, characterization methods, and mechanisms of drug delivery. In addition, their applications in cancer therapy, infectious diseases, chronic disorders, and gene therapy are explored. Nano-bio hybrid systems demonstrate improved targeting efficiency, reduced toxicity, and controlled drug release owing to the incorporation of biomolecules such as proteins, lipids, and nucleic acids. Recent advances, including smart nanocarriers, artificial intelligence-assisted design, and theranostic applications, have further expanded their clinical potential. In conclusion, nano-bio hybrid systems represent a promising strategy for personalized medicine by enabling patient-specific therapy with enhanced safety and efficacy. Despite challenges related to scalability and regulatory approval, ongoing research is expected to facilitate their clinical translation in the near future.

Keywords: Nano-bio hybrids, Targeted drug delivery, Personalized medicine, Nanotechnology, Theranostics

1. Introduction

Drug delivery systems have undergone a remarkable transformation from conventional dosage forms to advanced nanocarrier-based systems designed to improve therapeutic efficiency and patient compliance. Traditional drug delivery approaches often suffer from limitations such as poor solubility, low bioavailability, rapid metabolism, and lack of specificity, which result in reduced therapeutic efficacy and increased adverse effects (1-4). These challenges have driven the need for innovative strategies that enable precise and controlled drug delivery. Nanotechnology has emerged as a revolutionary approach in pharmaceutical sciences, offering nanoscale systems capable of improving drug solubility, stability, and bioavailability. Various nanocarriers, including liposomes, polymeric nanoparticles, dendrimers, and nanosuspensions, have demonstrated significant potential in overcoming biological barriers and enhancing drug delivery (5-8). However, despite these advantages, conventional nanocarriers may lack biological recognition capabilities and may be subjected to rapid clearance by the immune system (9-11).

To address these limitations, nano-bio hybrid systems have been developed by integrating synthetic nanomaterials with biological components such as proteins, lipids, nucleic acids, and cell membranes. These systems combine the structural advantages of nanomaterials with the functional specificity of biological entities, resulting in improved targeting efficiency and biocompatibility (3,13). The incorporation of biological components enables these systems to mimic natural biological processes, thereby enhancing their interaction with cells and tissues. Nano-bio hybrid systems have significant implications in targeted and personalized medicine, where therapies are tailored according to individual patient characteristics and disease profiles. By enabling precise drug delivery and minimizing off-target effects, these systems improve therapeutic outcomes and reduce toxicity (4,14). This review aims to provide a comprehensive understanding of nano-bio hybrid systems, including their types, preparation methods, characterization techniques, mechanisms of action, applications, and prospects.

2. Overview of nano-bio hybrid systems

Nano-bio hybrid systems are advanced drug delivery platforms that combine engineered nanomaterials with biological molecules to enhance therapeutic performance. These systems typically consist of a nanocarrier core that provides structural support and drug loading capacity, along with a biological interface that facilitates targeting and interaction with specific cells (5,15). The integration of these components allows for improved stability, biocompatibility, and targeting efficiency. The working principle of nano-bio hybrid systems involves the encapsulation or conjugation of drugs within the nanocarrier, followed by targeted delivery to the desired site of action. Upon administration, these systems circulate in the body and accumulate at the target site through passive targeting mechanisms such as the enhanced permeability and retention effect, or through active targeting via ligand–receptor interactions (6,16). Controlled drug release ensures sustained therapeutic action and minimizes side effects. The design of nano-bio hybrid systems requires careful consideration of various factors, including particle size, surface charge, stability, drug loading capacity, and targeting efficiency. These parameters significantly influence the biodistribution, pharmacokinetics, and overall therapeutic effectiveness of the system (7,17). Proper optimization of these factors is essential for successful clinical application.

3. Types of nano-bio hybrid systems

Nano-bio hybrid systems encompass a wide range of platforms, including lipid–polymer hybrid nanoparticles, protein-based systems, cell membrane-coated nanoparticles, nucleic acid-based systems, and inorganic-biological hybrids. Lipid–polymer hybrid nanoparticles combine the advantages of polymeric nanoparticles and liposomes, providing structural stability and enhanced biocompatibility (8,18). These systems are widely used for controlled drug delivery and cancer therapy. Protein-based systems utilize biomolecules such as albumin and antibodies for drug delivery. These systems exploit the natural binding properties and biocompatibility of proteins to achieve targeted delivery and reduced immunogenicity (9,19). Cell membrane-coated nanoparticles represent an innovative approach in which nanoparticles are coated with natural cell membranes, enabling immune evasion and improved targeting (10,20). Nucleic acid-based hybrid systems are particularly important in gene therapy, where they facilitate the delivery of DNA, RNA, and gene-editing tools. These systems protect nucleic acids from degradation and enable efficient intracellular delivery (11,21). Inorganic-biological hybrids combine

inorganic nanoparticles such as gold or silica with biological molecules, providing unique functionalities such as imaging, photothermal therapy, and diagnostics (12,22).

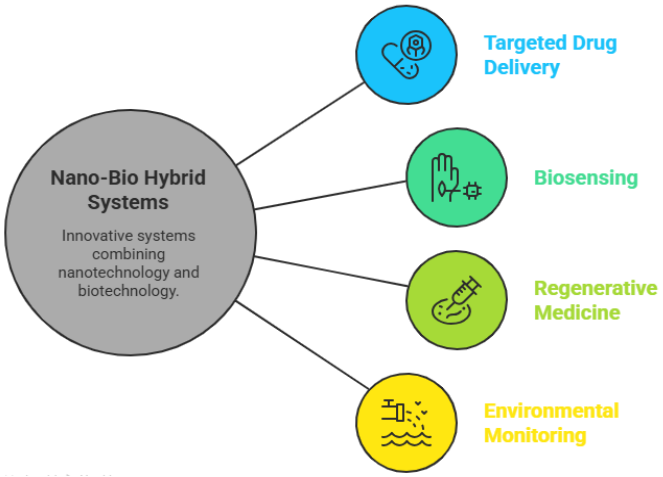

Figure 1. Diverse Platforms of Nano-Bio Hybrid Systems

4. Methods of preparation

Various methods are employed for the preparation of nano-bio hybrid systems, depending on the desired properties and applications. Nanoprecipitation is a commonly used technique in which a polymer and drug are dissolved in an organic solvent and then added to an aqueous phase, resulting in nanoparticle formation due to solvent diffusion (13,23). This method is simple and suitable for producing nanoparticles with a uniform size. Emulsification techniques involve the formation of emulsions followed by solvent evaporation to produce nanoparticles. This method is widely used for encapsulating hydrophobic drugs (14,24). Self-assembly is another important approach in which biomolecules spontaneously organize into stable nanostructures under specific conditions, driven by intermolecular interactions (15,25). Microfluidic methods provide precise control over particle size and reproducibility by manipulating fluids at the microscale. These techniques are highly efficient and suitable for large-scale production (16,26). Green synthesis methods utilize biological agents such as plant extracts or microorganisms to produce nanoparticles in an eco-friendly and sustainable manner (17,27).

5. Characterization techniques

Characterization of nano-bio hybrid systems is essential for evaluating their physicochemical and functional properties. Particle size and zeta potential are important parameters that influence stability and cellular uptake, and are typically measured using dynamic light scattering techniques (18,28). Morphological analysis using scanning electron microscopy and transmission electron microscopy provides detailed information on particle shape and structure. Drug loading and encapsulation efficiency are critical parameters that determine the amount of drug incorporated into the system, and are evaluated using spectroscopic and chromatographic methods (19,29). In vitro drug release studies are conducted to assess the release kinetics and mechanism of drug delivery (20,30). Stability studies are performed to evaluate the physical and chemical stability of the formulation under various conditions (21,31).

Figure 2. Characterization Techniques of Nano-Bio Hybrid Systems Showing Physicochemical and Functional Evaluation Parameters Including Particle Size, Zeta Potential, Morphology, Drug Loading, *In Vitro* Drug Release, and Stability Studies

6. Mechanism of drug delivery

Nano-bio hybrid systems facilitate drug delivery through a combination of sophisticated mechanisms, including passive targeting, active targeting, stimuli-responsive release, and cellular uptake, which collectively enhance therapeutic efficacy and precision. Passive targeting primarily depends on the enhanced permeability and retention (EPR) effect, a phenomenon commonly observed in tumor tissues. Due to rapid angiogenesis, tumor vasculature is often irregular and leaky, allowing nanoparticles of appropriate size to extravasate and accumulate preferentially in tumor sites. Additionally, impaired lymphatic drainage in tumor tissues further promotes the retention of these nanoparticles, leading to increased local drug concentration and improved therapeutic outcomes (22,32). In contrast, active targeting involves the functionalization of nano-bio hybrid systems with specific ligands such as antibodies, peptides, aptamers, or small molecules that can selectively bind to receptors overexpressed on target cells. This ligand–receptor interaction enhances the specificity of drug delivery, facilitating receptor-mediated endocytosis and improving cellular internalization. Active targeting not only increases drug accumulation at the desired site but also minimizes off-target effects, thereby reducing systemic toxicity and enhancing treatment efficiency (23,33).

Another important mechanism is stimuli-responsive drug release, which allows nano-bio hybrid systems to release their therapeutic payload in response to specific internal or external triggers. Internal stimuli include variations in pH, redox potential, and enzyme activity, which are often characteristic of diseased tissues such as tumors or inflamed regions. External stimuli such as temperature, light, magnetic fields, or ultrasound can also be applied to trigger drug release in a controlled manner. This approach ensures site-specific and on-demand drug release, thereby improving therapeutic precision and reducing unintended side effects (24,34). Cellular uptake of nano-bio hybrid systems occurs predominantly through endocytosis, a process by which cells internalize nanoparticles into intracellular compartments. Depending on the size, surface properties, and composition of the nanoparticles, different endocytic pathways such as clathrin-mediated, caveolae-mediated, or macropinocytosis may be involved. Once internalized, the nanoparticles can escape from endosomes and release their drug payload within the cytoplasm or specific organelles, enabling effective intracellular drug delivery. This mechanism is particularly important for the delivery of biomolecules such as proteins and nucleic acids, which require intracellular localization for their therapeutic action (25,35).

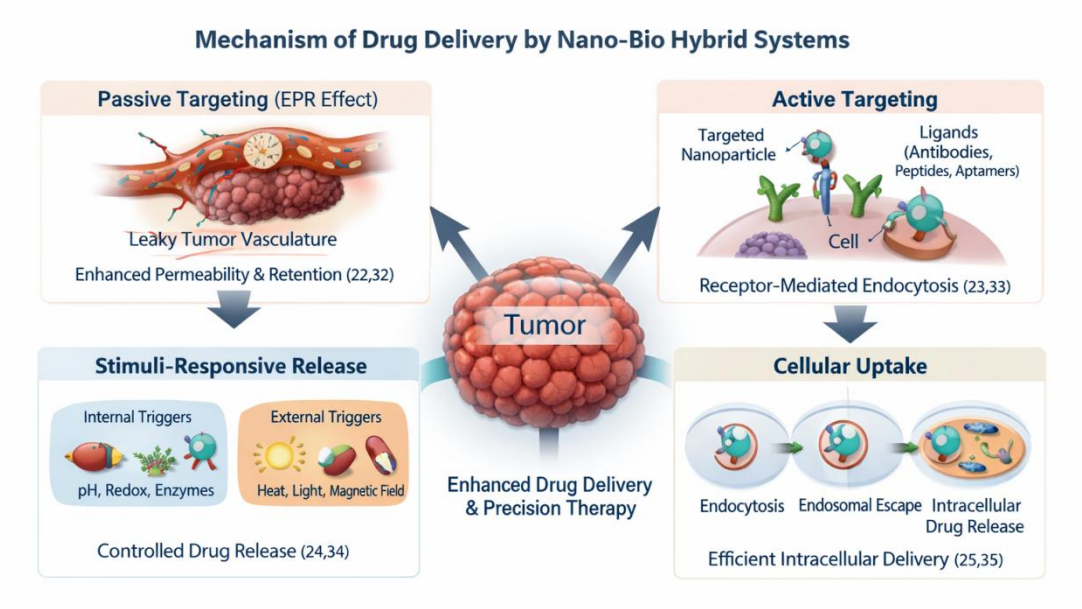

Figure 3: Mechanisms of Nano-Bio Hybrid Drug Delivery

7. Applications

Nano-bio hybrid systems have emerged as highly versatile platforms with extensive applications across multiple areas of medicine, owing to their ability to integrate the advantages of nanotechnology with biological specificity. In cancer therapy, these systems play a pivotal role in improving the delivery of chemotherapeutic agents by enabling targeted accumulation at tumor sites while minimizing exposure to healthy tissues. The incorporation of targeting ligands and biomimetic components enhances tumor selectivity and facilitates efficient cellular uptake, thereby reducing systemic toxicity and improving therapeutic efficacy. Furthermore, nano-bio hybrid systems can be engineered to overcome multidrug resistance mechanisms commonly observed in cancer cells, enhancing drug retention and effectiveness (26,36). In the treatment of infectious diseases, nano-bio hybrid systems offer significant advantages by improving the delivery and bioavailability of antimicrobial agents. These systems can penetrate biological barriers and deliver drugs directly to the site of infection, thereby increasing local drug concentration and enhancing antimicrobial activity. Additionally, they can be designed to bypass resistance mechanisms such as efflux pumps and biofilm formation, which are major challenges in conventional antimicrobial therapy. As a result, nano-bio hybrid systems contribute to overcoming antimicrobial resistance and improving treatment outcomes in bacterial, viral, and fungal infections (27,37).

In chronic diseases such as diabetes and cardiovascular disorders, nano-bio hybrid systems provide sustained and controlled drug release, which is essential for long-term disease management. By maintaining consistent drug levels in the bloodstream, these systems reduce the frequency of dosing and improve patient compliance. For instance, in diabetes management, they can enable prolonged insulin delivery, while in cardiovascular diseases, they facilitate targeted delivery of drugs to affected tissues, thereby enhancing therapeutic efficiency and minimizing side effects (28,38). In the field of gene therapy, nano-bio hybrid systems have shown remarkable potential as carriers for the delivery of genetic material such as DNA, RNA, and gene-editing tools. These systems protect nucleic acids from enzymatic degradation and enable efficient intracellular delivery, which is crucial for successful gene expression or gene silencing. By facilitating precise gene modulation, nano-bio hybrid systems offer promising strategies for the treatment of genetic disorders, cancer, and other complex diseases, thereby expanding the scope of advanced therapeutics (29,39).

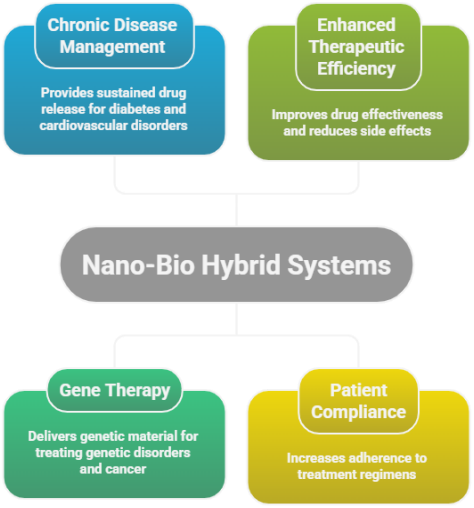

Figure 4. Applications and Benefits of Nano-Bio Hybrid Systems

8. Role in personalized medicine

S. No.	Aspect	Description	References
1	Personalized Therapeutic Strategies	Nano-bio hybrid systems enable the development of patient-specific therapeutic approaches based on individual genetic, molecular, and physiological characteristics.	(30, 40)
2	Targeted Drug Delivery	These systems are engineered to target specific biomarkers on diseased cells, ensuring precise and selective drug delivery while reducing off-target effects.	(30, 40)
3	Improved Treatment Accuracy	By focusing on disease-specific molecular signatures, nano-bio hybrid systems enhance therapeutic outcomes and accuracy.	(30, 40)
4	Theranostic Capability	Integration of diagnostic and therapeutic functions allows real-time monitoring of treatment response and therapy adjustment.	(30, 40)
5	Adaptive Treatment Design	Enables clinicians to customize treatment regimens based on genetic profile, disease progression, and patient response.	(30, 40)
6	Precision Drug Delivery	Ensures delivery of the right drug, at the right dose, to the right patient at the right time.	(30, 40)
7	Application in Complex Diseases	Facilitates targeted therapies for heterogeneous diseases like cancer, addressing individual variations in treatment response.	(30, 40)
8	Reduced Adverse Effects	Minimizes side effects while maximizing therapeutic efficiency, improving safety profile.	(30, 40)
9	Enhanced Patient Compliance	Improved safety and effectiveness lead to better patient adherence and quality of life.	(30, 40)
10	Advancement in Healthcare	Represents a major step toward safer, more effective, and individualized healthcare solutions.	(30, 40)

9. Advantages

Nano-bio hybrid systems offer a wide range of advantages that make them highly promising in modern drug delivery and therapeutic applications. One of the most significant benefits is their ability to improve the bioavailability of drugs, particularly those that are poorly water-soluble or unstable under physiological conditions. By encapsulating such drugs within nanocarriers and protecting them from degradation, these systems enhance drug stability and ensure efficient delivery to the target site. Additionally, the incorporation of biological components such as proteins, lipids, or cell membranes enhances biocompatibility and reduces the likelihood of immune recognition, thereby prolonging circulation time in the bloodstream. Another important advantage of nano-bio hybrid systems is their enhanced target specificity. Through the use of targeting ligands such as antibodies, peptides, or aptamers, these systems can selectively bind to specific receptors expressed on diseased cells. This targeted approach not only increases the accumulation of drugs at the desired site but also minimizes exposure to healthy tissues, thereby significantly reducing systemic toxicity. Furthermore, the ability of these systems to facilitate receptor-mediated uptake enhances intracellular drug delivery, which is particularly beneficial in the treatment of diseases such as cancer and genetic disorders.

Controlled and sustained drug release is another key feature of nano-bio hybrid systems. By carefully designing the composition and structure of the nanocarrier, it is possible to regulate the rate and duration of drug release, ensuring consistent therapeutic levels over an extended period. This reduces the need for frequent dosing and improves patient compliance. Moreover, stimuli-responsive properties can be incorporated to enable site-specific and on-demand drug release in response to environmental triggers such as pH or temperature. Overall, the integration of synthetic nanomaterials with biological components results in synergistic effects that enhance therapeutic performance beyond that of conventional drug delivery systems. These advantages collectively contribute to improved efficacy, safety, and patient outcomes, making nano-bio hybrid systems a superior alternative in advanced drug delivery applications (31,41).

10. Limitations and challenges

Despite their numerous advantages, nano-bio hybrid systems face several limitations and challenges that hinder their widespread clinical application. One of the primary concerns is the potential toxicity associated with nanomaterials. While many nanocarriers are designed to be biocompatible, certain materials may induce cytotoxicity, oxidative stress, or immune responses, particularly when used at higher concentrations or over prolonged periods. The long-term safety and biodistribution of these systems remain areas of active investigation, necessitating thorough toxicological evaluation before clinical use. Stability is another significant challenge in the development of nano-bio hybrid systems. These systems may undergo physical or chemical changes during storage or upon exposure to physiological conditions, leading to aggregation, premature drug release, or loss of functionality. Maintaining the integrity of both the nanocarrier and the biological components is critical to ensuring consistent performance and therapeutic efficacy.

Large-scale production and reproducibility also present major obstacles. Many preparation techniques used at the laboratory scale are difficult to translate into industrial-scale manufacturing due to issues related to cost, complexity, and variability. Achieving uniform particle size, consistent drug loading, and batch-to-batch reproducibility remains a challenge, which can impact the quality and reliability of the final product. In addition to technical challenges, regulatory hurdles significantly limit the clinical translation of nano-bio hybrid systems. The lack of standardized guidelines for evaluating their safety, efficacy, and quality poses difficulties for approval by regulatory authorities. Furthermore, the complex nature of these systems, involving both synthetic and biological components, complicates their classification and assessment under existing regulatory frameworks. Overall, while nano-bio hybrid systems hold immense potential, addressing these challenges is essential for their successful development and commercialization. Continued research, improved manufacturing techniques, and the establishment of clear regulatory guidelines are crucial to overcoming these limitations and enabling their widespread clinical adoption (32,42).

11. Recent advances

Recent advances in nano-bio hybrid systems have significantly expanded their potential in targeted drug delivery and personalized medicine, driven by innovations in materials science, biotechnology, and computational approaches. One of the most notable developments is the emergence of smart nanocarriers that are capable of responding to specific environmental stimuli. These advanced systems are engineered to detect and react to internal triggers such as pH variations, redox gradients, and enzyme activity, which are commonly associated with diseased tissues, particularly tumors and inflamed regions. Upon encountering such stimuli, the nanocarriers undergo structural or chemical changes that enable controlled and site-specific release of the therapeutic payload, thereby enhancing treatment precision and minimizing systemic side effects. In addition to internal triggers, external stimuli such as temperature, light, ultrasound, and magnetic fields are also being utilized to achieve spatiotemporal control over drug release, further improving therapeutic outcomes (33,43). Another significant advancement in this field is the integration of artificial intelligence (AI) and machine learning techniques in the design and optimization of nano-bio hybrid systems. AI-driven platforms are increasingly being used to predict physicochemical properties, drug–carrier interactions, and biological responses, thereby accelerating the development process and reducing experimental costs. These computational tools enable the rational design of nanocarriers with optimized size, surface characteristics, and targeting efficiency, ultimately improving their performance in clinical applications. The use of big data and predictive modeling also facilitates the identification of suitable biomarkers and therapeutic targets, contributing to more precise and effective drug delivery strategies (33,43).

Theranostic systems represent another breakthrough in nano-bio hybrid technology. These systems integrate diagnostic and therapeutic functionalities into a single platform, enabling simultaneous disease detection, monitoring, and treatment. For example, nanoparticles can be designed to carry imaging agents along with therapeutic drugs, allowing real-time tracking of drug distribution and therapeutic response. This dual functionality not only enhances treatment efficacy but also supports personalized medicine by enabling clinicians to adjust therapy based on patient-specific responses. The development of multifunctional theranostic platforms has opened new avenues for early disease diagnosis, targeted therapy, and improved clinical outcomes (34,44).

12. Future perspectives

The future of nano-bio hybrid systems is highly promising, with significant potential for transforming modern healthcare through their integration into clinical practice. Continued advancements in nanotechnology, biotechnology, and material science are expected to further enhance the functionality, safety, and efficiency of these systems. One of the emerging areas of interest is nanorobotics, where nanoscale devices are designed to perform specific tasks within the human body, such as targeted drug delivery, disease detection, and tissue repair. These nanorobots, when combined with biological components, could enable highly precise and controlled therapeutic interventions, representing a major leap forward in medical technology. In addition to nanorobotics, the development of advanced biomaterials is expected to play a crucial role in the evolution of nano-bio hybrid systems. Novel biomaterials with improved biocompatibility, biodegradability, and functional versatility are being explored to enhance the performance of hybrid systems. These materials can be engineered to interact more effectively with biological systems, thereby improving targeting efficiency and reducing adverse effects. Furthermore, the incorporation of responsive and adaptive materials will enable the development of next-generation systems capable of dynamically adjusting to changing physiological conditions.

Interdisciplinary collaboration among researchers from fields such as pharmaceutics, nanotechnology, molecular biology, and computational sciences will be essential to drive innovation in this area. Such collaborative efforts will facilitate the translation of laboratory-scale developments into clinically viable products. Moreover, advancements in regulatory frameworks and standardization will be necessary to ensure the safe and effective implementation of these systems in healthcare. Overall, nano-bio hybrid systems are expected to play a central role in the future of precision medicine by enabling highly targeted, efficient, and patient-specific therapies. With ongoing research and technological progress, these systems hold the potential to revolutionize disease management and significantly improve global healthcare outcomes (35).

13. Conclusion

Nano-bio hybrid systems represent a transformative approach in modern drug delivery and personalized medicine. By integrating nanotechnology with biological components, these systems offer enhanced targeting, improved therapeutic efficacy, and reduced toxicity. They have demonstrated significant potential in various applications, including cancer therapy, gene delivery, and chronic disease management. Despite existing challenges such as toxicity concerns, scalability issues, and regulatory barriers, ongoing research and technological advancements are addressing these limitations. Recent developments in smart nanocarriers, artificial intelligence-based design, and theranostic applications have further expanded their potential. As research progresses, nano-bio hybrid systems are expected to play a crucial role in precision medicine by enabling patient-specific treatment strategies. Overall, these systems represent a new frontier in healthcare with promising clinical implications.

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