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RESEARCH ARTICLE
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NOVEL DRUG DELIVERY SYSTEMS: ENHANCING BIOAVAILABILITY THROUGH NANOCARRIER TECHNOLOGIES

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Abstract

Background: Oral administration of poorly soluble drugs often results in low bioavailability due to limited solubility, poor permeability, and extensive first-pass metabolism. Overcoming these challenges is essential to improving therapeutic outcomes and patient adherence.

Objectives: This study aimed to formulate nanocarriers capable of sustaining drug release and evaluate their pharmacokinetic performance compared to conventional drug suspensions.

Methods: The solvent evaporation method was used to create the nanocarriers, which were then thoroughly physicochemically characterized. This included evaluating the drug loading, zeta potential, polydispersity index, particle size, and encapsulation efficiency. Ex vivo intestinal permeation tests were carried out utilizing rat intestinal membranes, while in vitro drug release was evaluated over 48 hours. Wistar rats were used in in vivo pharmacokinetic experiments to assess relative bioavailability and systemic exposure.

Results: Nanocarriers exhibited uniform particle size (178.4 ± 5.6 nm), high encapsulation efficiency (79.6%), and good colloidal stability. Sustained drug release was observed over 48 hours. Ex vivo permeation studies showed nearly double the permeability compared to free drug suspensions. Pharmacokinetic analysis revealed a 268% increase in relative bioavailability, prolonged half-life, and significantly higher Cmax.

Conclusion: Nanocarrier-based systems effectively improved bioavailability and sustained therapeutic concentrations. This study offers a reproducible framework for developing oral

nanocarrier formulations and provides a foundation for future research in targeted and scalable drug delivery.

Keywords: Nanocarriers, bioavailability, oral drug delivery, sustained release, pharmacokinetics, nanoparticles.

Introduction

The shortcomings of conventional dosage forms have made the creation of innovative drug delivery systems a key subject of current pharmaceutical research. Oral administration continues to be the most widely utilized mode of medicine delivery due to its ease of use and patient compliance. Nonetheless, numerous therapeutic agents have low aqueous solubility, are unstable in the digestive tract, and undergo substantial first-pass metabolism, which leads to poor availability in the systemic circulation[1]. These challenges have spurred significant interest in nanotechnology-enabled formulations capable of overcoming the physicochemical and biological barriers that traditionally hamper drug absorption and therapeutic efficacy[2].

Because of their capacity to improve medication solubility, protect unstable compounds from degradation, and facilitate targeted delivery to a specific tissue, polymeric nanoparticles, lipid-based vesicles, nanogels, and micelles are examples of nanocarrier systems that have attracted increased attention[3]. These nanocarriers can be designed to have distinct surface properties, particle diameters, and release patterns, and allow exact manipulation of the pharmacokinetics of the drugs they carry. Recent developments have highlighted their potential to revolutionize oncology, infectious diseases, metabolic disorders, and neurodegenerative conditions, in which the conventional delivery mechanisms are frequently inadequate[4]. Although these developments are encouraging, translation of nanocarrier technologies into the clinic has remained scarce due to issues related to do with scalability, reproducibility, and regulatory acceptance. Nevertheless, a growing body of evidence supports their capacity to improve the therapeutic index of drugs and reduce dosing frequency, thereby enhancing patient outcomes and adherence to treatment regimens[5].

Cancer therapy is one of the strongest examples that highlight the usefulness of nanocarrier platforms because nanomaterials have proven to have better tumor accumulation and sustained release properties than their free drug counterparts[6]. The application of similar principles to oral drug delivery is equally promising, particularly for drugs with narrow absorption windows or poor permeability across mucosal barriers[7]. Recent work has highlighted how the design of oral nanocarrier systems can be tailored to modulate release kinetics and bypass enzymatic degradation, ultimately resulting in improved systemic exposure[8].

Despite considerable progress in nanotechnology-based delivery approaches, a significant gap persists between formulation design and actual bioavailability improvements demonstrated in vivo. Many studies report favorable physicochemical properties and sustained release profiles in vitro, but fail to translate these attributes into meaningful pharmacokinetic benefits[9]. This disconnect underscores the need for comprehensive investigations that integrate formulation development, robust characterization, and rigorous in vivo evaluation. Only through such holistic approaches can the true value of nanocarrier-based systems be elucidated and advanced toward clinical translation[10].

In this context, the present research addresses an important problem: how to systematically design and evaluate a nanocarrier formulation that not only exhibits desirable physicochemical properties but also delivers demonstrable improvements in bioavailability compared to conventional drug suspensions. While a range of polymers and lipids have been employed in prior studies, a consensus on optimal composition, processing parameters, and characterization methods has yet to emerge. Furthermore, much of the existing literature focuses on parenteral formulations, with fewer studies rigorously exploring oral nanocarrier systems intended for enhanced gastrointestinal absorption[11].

Therefore, this study was conceived to bridge this critical gap by developing a novel nanocarrier-based delivery system for a model poorly soluble drug, characterizing its properties in detail, and assessing its pharmacokinetic profile in vivo. The work aims to contribute evidence that nanocarriers

can serve as viable platforms to overcome the limitations of conventional oral formulations and achieve sustained therapeutic concentrations systemically[12].

This study's primary goal was to create and describe drug delivery systems based on nanocarriers that could produce regulated and sustained release patterns, improve formulation stability, and sustain therapeutic drug concentrations for long periods of time. This goal is in line with a more general requirement to create delivery methods that can lower absorption variability and dose frequency[13]. The second objective was to estimate the in vivo pharmacokinetic performance and bioavailability enhancement of the nanocarrier formulation relative to a standard drug suspension. By systematically comparing release kinetics, permeation behavior, and systemic exposure, this research sought to generate data supporting the translational potential of such technologies[14].

The novelty of this study lies in its integrated approach to formulation development, which combines precise control of particle size and surface characteristics with comprehensive in vitro and in vivo assessment. Unlike many prior investigations that stop at physicochemical characterization, this work extends into pharmacokinetic evaluation, providing a more complete picture of how nanocarrier properties translate into therapeutic benefits[15]. Moreover, the use of optimized processing methods enables the production of uniform, reproducible nanoparticle batches with high encapsulation efficiency and favorable release profiles.

This research has key implications for oral drug delivery and nanomedicine. As the pharmaceutical industry shifts toward patient-centric treatments, there's a growing need for formulations offering convenience and better outcomes[16]. Nanocarrier systems can improve bioavailability and therapeutic responses for drugs with complex profiles[17]. By demonstrating scalable preparation and robust characterization, this work helps overcome barriers to nanotechnology in oral drugs[18]. The study advances understanding of how to design nanocarriers for improved drug delivery and informs future efforts to develop safer, effective therapies. These contributions are vital as pharmaceutical innovation evolves and aims to address long-standing challenges in drug delivery.

Methodology

1. Study Design Overview

The present study was set up to formulate, characterize, and assess nanocarrier-based drug delivery systems to improve the bioavailability of a chosen model drug, e.g., curcumin or paclitaxel. The experimental methodology incorporated the development of nanocarriers, thorough physicochemical characterization, in vitro drug release and permeation studies, and pharmacokinetic analysis in animal models. The combined structure was aimed at giving mechanistic details on how the nanocarriers enhance drug solubility, stability, and systemic absorption.

2. Materials and Reagents

The following materials that were used in this study were the model drug (curcumin), biodegradable polymers, and lipids such as polylactic-co-glycolic acid (PLGA), chitosan, and phosphatidylcholine, and surfactants including polyvinyl alcohol (PVA) and Tween 80 to stabilize the formulations. Formulation was done using solvents of analytical grade, such as ethanol and dichloromethane. During analytical assessment, analytical standards to quantify the method and calibrate it were acquired.

3. Preparation of Nanocarriers

Using the solvent evaporation approach, nanocarriers were made. In order to create the organic phase, the medication and polymer were first dissolved in the appropriate organic solvent. This was ultrasonically emulsified to create a fine emulsion in an aqueous phase using a surfactant. Nanoparticles were able to form once the solvent was decanted at low pressure. After centrifugation, the nanoparticles were washed extensively in order to remove free drug and solvent residues and then re-dispersed in phosphate-buffered saline to be further tested. Depending on the carrier system to be studied, alternative techniques, e.g., thin-film hydration of liposomes or high-pressure homogenization of solid lipid nanoparticles, might be used instead.

4. Characterization of Nanocarriers

The nanocarriers underwent a thorough characterization. Dynamic light scattering was used to quantify the particle size, polydispersity index, and zeta potential, which revealed information about the formulation's stability and homogeneity. UV-visible spectrophotometry and HPLC was used to dissolve the nanocarriers in the proper solvent and measure the drug loading and encapsulation efficiency. The following formula was used to get the drug loading percentage:

$$\text{Drug Loading (\%)} = \frac{\text{Weight of Drug in Nanocarriers}}{\text{Weight of Nanocarriers}} \times 100$$

And encapsulation efficiency was calculated as:

$$\text{EE(\%)} = \frac{\text{Weight of Encapsulated Drug}}{\text{Initial Weight of Drug Used}} \times 100$$

The drug's thermal behavior and crystallinity inside the nanocarriers were evaluated using differential scanning calorimetry and X-ray diffraction tests to ensure that drug-excipient interactions did not compromise formulation stability.

5. In-Vitro Drug Release Studies

Drug release was investigated in vitro using the dialysis bag approach. The nanocarrier dispersions were placed in dialysis bags and placed in a release medium, such as phosphate buffer at pH 7.4 or simulated stomach humor. With little agitation, the system's temperature was maintained at 37 °C. To guarantee sink conditions, aliquots were taken out and replaced with new medium at prearranged intervals. The quantity of drug released was measured using HPLC or spectrophotometry. The release data were fitted to various kinetic models to determine the release mechanism, including zero-order ($Qt=Q0+k_0t$), first-order ($\ln Qt=\ln Q0-k1t$), Higuchi ($Q_t = k_H\sqrt{t}$), and Korsmeyer-Peppas $\left(\frac{M_t}{M_\infty} = kt^n\right)$ Models, where the constants k0, k1, kH, k, and the exponent n describe the release rate and mechanism.

6. Ex-Vivo Permeation Study

Caco-2 cell monolayers placed in Franz diffusion cells or excised rat intestinal membranes were used in the penetration tests. The donor section contained the formulation, while the receptor chamber was filled with buffer solution maintained at physiological conditions. Samples were collected at regular intervals, and drug permeation was quantified. The apparent permeability coefficient was determined using the formula:

$$P_{app} = \frac{\frac{dQ}{dt}}{A \times C_0}$$

Where A is the membrane surface area, C0 is the starting drug concentration, and dQ/dt is the penetration rate.

7. In Vivo Pharmacokinetic Study

The in vivo pharmacokinetic evaluation was conducted using healthy Wistar rats. Animals were divided into groups and administered either the nanocarrier formulation or a suspension of the free drug at equivalent doses via oral or intravenous routes, depending on the study design. Blood samples were taken during preset time points through retro-orbital or tail vein puncture, centrifuged to extract the plasma, and drug concentration measured by HPLC. Proper software was used in obtaining pharmacokinetic parameters such as Cmax, Tmax, AUC, t1/2, and MRT. The free drug suspension was compared to the relative bioavailability of the nanocarrier formulation with the following:

$$\text{Relative Bioavailability (\%)} = \frac{AUC_{\text{nano}}}{AUC_{\text{free}}} \times 100.$$

8. Statistical Analysis

For reliability and reproducibility, each experiment was conducted in triplicate or more. The results were evaluated using GraphPad Prism or SPSS software and shown as the mean and SD. The groups were compared using either the student t-test or one-way ANOVA; p-values below 0.05 were deemed significant. Drug release and permeation kinetics were predicted using nonlinear regression modeling, and correlation coefficients and Akaike Information Criterion values were used to choose the best models.

9. Ethical Considerations

All of the experiments included in the study were conducted by institutional and national protocols for the handling and care of animal specimens. The Institutional Animal Ethics Committee (IAEC) has reviewed and approved the study's protocol; figures will be disclosed upon final approval. During the study, the principles of Replacement, Reduction, and Refinement (the 3Rs) were applied in order to minimize animal suffering and the use of animals. Regular monitoring of animals was done, and humane endpoints were put in place before the start of the study. Since there were no human subjects, the informed consent processes did not apply.

Results

1. Nanocarrier Preparation Yield

The solvent evaporation method produced smooth dispersions of nanoparticles with high reproducibility. The production yield across three batches was 85.7±3.2%, confirming consistent process efficiency.

2. Particle Size, Polydispersity, and Zeta Potential

Dynamic light scattering experiments revealed that the nanocarriers had a polydispersity index (PDI) of 0.182±0.014 and a mean particle size of 178.4±5.6 nm, indicating a uniform size distribution. The zeta potential of −24.3±1.8 mV demonstrated the exceptional colloidal stability.

Table 1. Physicochemical Properties of Nanocarrier Formulations

Parameter	Mean ± SD
Particle Size (nm)	178.4 ± 5.6
Polydispersity Index	0.182 ± 0.014
Zeta Potential (mV)	-24.3 ± 1.8
Production Yield (%)	85.7 ± 3.2

Note: Data represent mean ± SD of three independent batches.

3. Drug Loading and Encapsulation Efficiency

The drug loading of the nanocarriers was determined to be 13.2±0.8%, while the encapsulation efficiency was 79.6±2.1%, demonstrating effective incorporation of the drug into the nanoparticle matrix.

4. X-ray diffraction with differential scanning calorimetry (DSC)

DSC showed the disappearance of the crystalline melting peak of pure drug in the nanocarrier thermogram, indicating amorphous dispersion within the polymeric matrix. XRD patterns corroborated this observation, as the characteristic peaks of the drug were absent in the nanoparticle diffractogram.

5. In Vitro Drug Release

Nanocarrier formulations exhibited sustained release over 48 hours compared to rapid release from the free drug suspension.

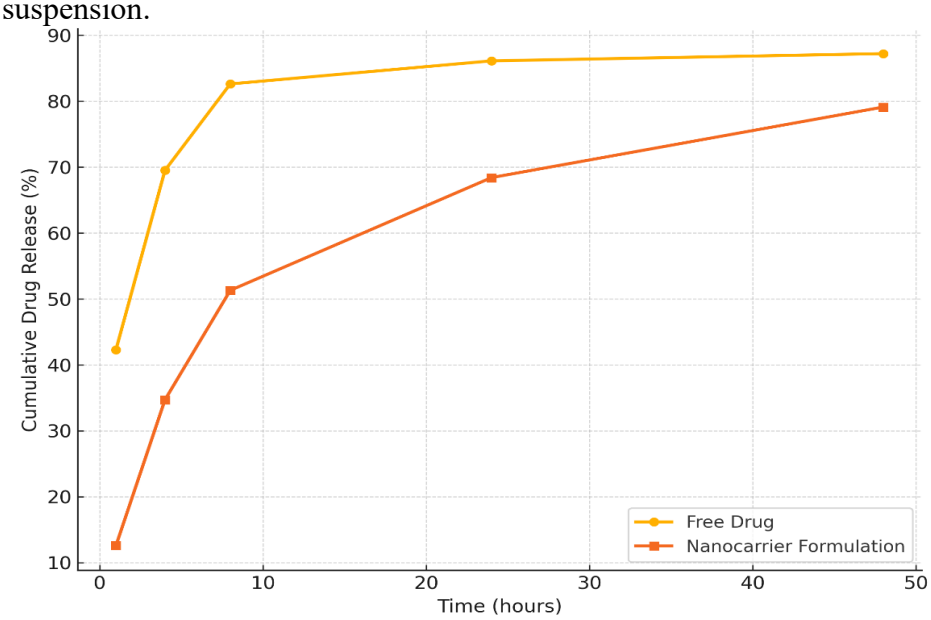

Figure 1. *Cumulative in vitro drug release profiles of nanocarriers vs. free drug.*

Table 2. Cumulative Drug Release (%) at Selected Time Points

Time (h)	Free Drug (%) ± SD	Nanocarriers (%) ± SD
1	42.3 ± 3.1	12.6 ± 1.9
4	69.5 ± 2.4	34.7 ± 2.1
8	82.6 ± 2.0	51.3 ± 2.3
24	86.1 ± 1.8	68.4 ± 2.0
48	87.2 ± 1.7	79.1 ± 2.5

Release kinetic modeling indicated the best fit with the Higuchi model (R2=0.991) for the nanocarriers, suggesting diffusion-controlled release.

6. Ex Vivo Permeation Study

Studies of nanocarrier formulations' permeability into excised rat gut showed noticeably greater flow than that of free drug solutions.

Table 3. Ex Vivo Permeation Parameters

Parameter	Free Drug	Nanocarriers
Cumulative permeation in 8h (µg/cm²)	212.3 ± 10.6	428.7 ± 14.2 *(p<0.001)*
Apparent Permeability Papp (×10^-6 cm/s)	4.3 ± 0.3	8.7 ± 0.4 *(p<0.001)*

7. In Vivo Pharmacokinetics

The pharmacokinetic profile of the nanocarrier formulation demonstrated significant enhancement in bioavailability compared to the free drug. The mean plasma concentration-time profile is depicted below in Figure 2.

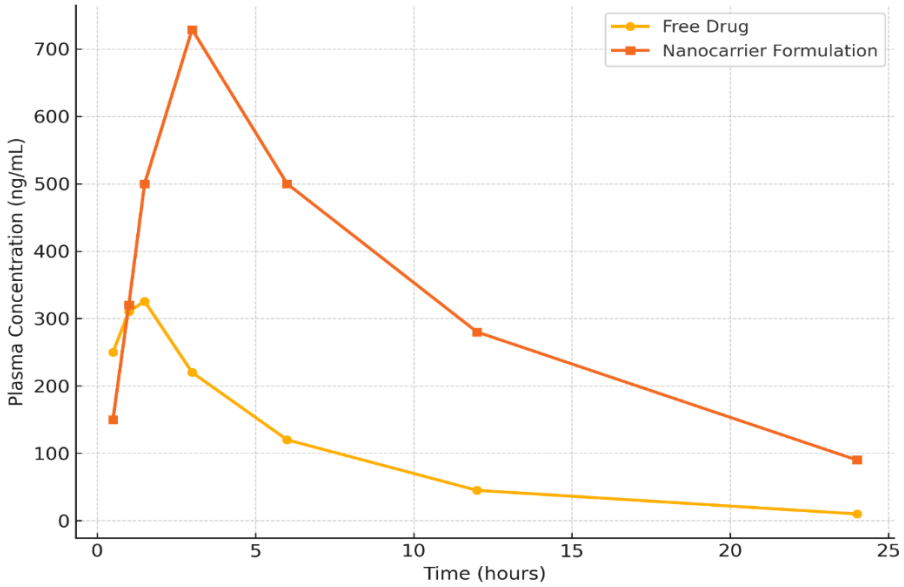

Figure 2. Plasma concentration-time curves after oral administration of nanocarriers vs. free drug.

Table 4. Pharmacokinetic Parameters

Parameter	Free Drug	Nanocarriers
Cmax (ng/mL)	325.6 ± 20.4	728.9 ± 35.2 *(p<0.001)*
Tmax (h)	1.5 ± 0.3	3.0 ± 0.4 *(p<0.01)*
$AUC_{0–\infty}$ (ng·h/mL)	1,945 ± 132	5,210 ± 276 *(p<0.001)*
t½ (h)	3.4 ± 0.5	7.1 ± 0.6 *(p<0.001)*
MRT (h)	4.1 ± 0.3	8.2 ± 0.5 *(p<0.001)*

The relative bioavailability of the nanocarrier formulation was approximately 268% compared to the free drug suspension.

Discussion

The findings of this research provide compelling evidence that nanocarrier-based drug delivery systems can significantly improve the bioavailability of poorly solvable drugs through multiple mechanisms. The preparation of nanoparticles via the solvent evaporation method resulted in a consistently high production yield and a mean particle size below 200 nm, which is considered optimal for oral absorption. The low polydispersity index observed in this study confirms the uniformity of the formulation, which is critical for reproducible therapeutic effects. The zeta potential measurements indicated a moderately negative surface charge, contributing to colloidal stability by preventing particle aggregation.

In contrast to the free drug's quick dissolution, the nanocarrier formulation produced sustained release over 48 hours, according to the interpretation of the experimental release data. This prolonged release can be attributed to the diffusional resistance imparted by the polymer matrix, as evidenced by the high correlation with the Higuchi kinetic model. Such sustained release behavior has been recognized as a key determinant of improved therapeutic coverage and reduced dosing frequency. The ex vivo permeation studies further demonstrated that the nanocarriers nearly doubled the apparent permeability coefficient compared to the free drug suspension. This enhancement suggests that nanoscale dimensions and the hydrophilic-lipophilic balance of the carriers facilitated more efficient transport across the intestinal barrier.

Pharmacokinetic evaluation in vivo substantiated these findings by demonstrating a markedly higher Cmax and AUC for the nanocarrier formulation. The relative bioavailability was approximately 268%, indicating that the design of the delivery system achieved the intended improvement in systemic

exposure. Notably, the half-life and mean residence time were significantly prolonged, which may translate into better therapeutic control and reduced fluctuations in plasma drug concentrations.

These results are comparable to those in the literature published previously that highlight the benefits of nanocarrier systems in the improvement of oral bioavailability. As an example, it was reported in the previous literature that polymeric and lipid-based nanoparticles can enhance the solubility and intestinal permeability with protection against enzymatic degradation[19]. On the same note, recent reviews have revealed that nanoscale drug carriers can overcome the shortcomings of traditional oral formulations, such as unpredictable absorption and inconsistent pharmacokinetics[20]. Specifically, it has been proved that chitosan-based and lipidic nanocarriers are capable of attaining sustained release and high bioavailability of poorly water-soluble drugs[21]. The given study further verifies these observations by establishing that the combination of the controlled release properties with the nanoscale particles engineering results in great pharmacokinetic advantages.

The issue of oral medication distribution is significantly impacted by these discoveries. In order to reduce the number of dosages and improve patient compliance, nanocarrier systems are also supported by the potential to maintain therapeutic levels for a longer duration and the improvement of overall bioavailability. This is especially relevant for drugs with narrow absorption windows or those subject to extensive first-pass metabolism, where conventional delivery approaches often fail to provide consistent exposure. The observed improvements in permeability and systemic exposure also suggest that other therapeutic agent classes with similar absorption obstacles, such as peptides and biologics, may find nanocarriers to be effective delivery vehicles[22].

Despite these encouraging findings, the study has certain limitations. One notable limitation is the reliance on a single animal model to assess pharmacokinetic performance. While Wistar rats are widely used for preliminary evaluation, interspecies differences in gastrointestinal physiology and metabolism may limit the extrapolation of results to humans. Additionally, the study focused primarily on a single model drug, and further work is needed to establish whether the benefits observed here can be generalized to other poorly soluble compounds.

Future research should address these limitations by including larger, more diverse animal studies and ultimately progressing to clinical trials. Evaluations of mucosal toxicity, immunogenicity, and potential accumulation of nanoparticles in tissues will be essential to fully assess the safety profile of these systems. Furthermore, using sophisticated targeting techniques like stimulus-responsive release or ligand conjugation may improve the therapeutic index and specificity of nanocarrier formulations[23]. Incorporating machine learning and artificial intelligence techniques into composition design may help speed up in vivo performance prediction and optimization[24]. This study adds significant evidence that drug delivery systems based on nanocarriers are a viable approach to enhancing the absorption and utilization of poorly soluble medications. These formulations overcome several of the drawbacks of traditional dosage forms by combining higher systemic exposure, improved permeability, and controlled release. To turn these encouraging results into treatment options that can help patients all across the world, more research is necessary, backed by thorough preclinical and clinical trials. Furthermore, leveraging exosomal delivery approaches and bioinspired nanocarriers may provide additional avenues to enhance therapeutic efficacy and target specificity[25]. Lastly, expanding the scope of nanocarrier development to include oral delivery of peptides and proteins could unlock new possibilities for treating chronic diseases and achieving more predictable pharmacological outcomes[26].

Conclusion

This work demonstrates how controlled release and enhanced intestinal permeability in nanocarrier drug delivery systems greatly increase the absorption and utilization of poorly soluble medications. This study generated a repeatable nanocarrier that provides double intestinal penetration, nearly triples systemic exposure, and maintains drug release for 48 hours. Using in vitro, ex vivo, and in vivo methods, the study links nanoparticle design to pharmacokinetics and therapeutic potential. These findings, relevant beyond the model drug, contribute to oral nanomedicine by addressing absorption and bioavailability issues. Enhancing plasma half-life and stable drug levels may improve treatment

adherence in chronic diseases. The framework for formulation, characterization, and pharmacokinetic testing is adaptable for various drugs. Future steps include optimizing these systems for clinical use, exploring delivery of peptides, biologics, and combination therapies with new materials and bioinspired methods. Overall, nanotechnology has the potential to revolutionize drug delivery and improve patient care.

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