J Nanostruct 14(1): 285-294, Winter 2024

RESEARCH PAPER

Enhanced Tumor Targeting: Curcumin-Loaded Chitosan Nanoparticles for Precision Drug Delivery: A Review

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ARTICLE INFO

Article History:
Received 02 October 2023
Accepted 17 December 2023
Published 01 January 2024

Keywords:
Chitosan
Curcumin
Drug Delivery
Nanoparticles

ABSTRACT

Curcumin, a naturally occurring polyphenol, has shown promising anti-cancer properties, but its clinical application is hindered by poor bioavailability. Chitosan nanoparticles (CHNPs) have emerged as a potential solution to enhance curcumin delivery due to their biocompatibility, biodegradability, and ability to facilitate targeted drug delivery. This review focuses on the development and application of curcumin-loaded chitosan nanoparticles (Cur-CHNPs) for precision cancer therapy. It highlights recent advances in synthesis methods, characterization, and mechanisms of tumor targeting. Additionally, the review discusses the in vitro and in vivo studies that demonstrate the efficacy of Cur-CHNPs, and explores future directions for improving cancer treatment.

How to cite this article
. *Enhanced Tumor Targeting: Curcumin-Loaded Chitosan Nanoparticles for Precision Drug Delivery: A Review. J Nanostruct, 2024; 14(1):285-294. DOI: 10.22052/JNS.2024.01.029*

INTRODUCTION

Cancer remains one of the leading causes of morbidity and mortality worldwide, presenting significant challenges in treatment due to the heterogeneity of the disease and the limitations of conventional therapies. Traditional chemotherapy and radiation therapy, while effective in some

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cases, often result in severe side effects and damage to healthy tissues. This has led to an increasing demand for more effective and selective treatment modalities that can target cancer cells while minimizing harm to normal cells [1]. Targeted drug delivery has emerged as a crucial strategy in the fight against cancer, offering the potential to increase the efficacy of therapeutic agents while reducing systemic toxicity. Among the various approaches to targeted drug delivery, nanoparticles have gained considerable attention due to their ability to enhance drug solubility, protect drugs from degradation, and facilitate controlled and targeted release [2]. Curcumin, a bioactive compound derived from the turmeric plant (Curcuma longa), has been extensively studied for its anti-inflammatory, antioxidant, and anti-cancer properties [3]. Despite its therapeutic potential, curcumin's clinical application is significantly limited by its poor aqueous solubility, rapid metabolism, and low systemic bioavailability. To overcome these challenges, researchers have explored various drug delivery systems, with chitosan nanoparticles emerging as a promising carrier for curcumin [4]. Chitosan, a natural polysaccharide obtained from chitin, possesses several favorable properties, including biocompatibility, biodegradability, and the ability to form nanoparticles. Chitosan nanoparticles (CHNPs) can encapsulate curcumin, thereby improving its solubility, stability, and bioavailability. Moreover, CHNPs can be engineered to achieve targeted drug delivery, making them an attractive platform for cancer therapy [5].

The aim of this review is to provide a comprehensive overview of the recent advancements in the development of curcumin-loaded chitosan nanoparticles (Cur-CHNPs) for precision cancer therapy. We will discuss the synthesis methods, characterization techniques, and mechanisms of tumor targeting associated with Cur-CHNPs. Additionally, we will explore the in vitro and in vivo studies that demonstrate the efficacy of Cur-CHNPs, compare them with other drug delivery systems, and highlight the challenges and future directions in this field. By presenting this information, we aim to underscore the novelty and potential of Cur-CHNPs as a targeted drug delivery system for enhancing cancer treatment outcomes.

CURCUMIN: PROPERTIES AND CHALLENGES

Chemical Structure and Properties of Curcumin

Curcumin, a naturally occurring polyphenolic compound, is the principal curcuminoid found in the rhizome of turmeric (Curcuma longa). Its chemical structure is identified as (1E,6E)-1,7-bis(4-hydroxy-3-methoxyphenyl)hepta-1,6-diene-3,5-dione, featuring two aromatic rings linked by a seven-carbon chain with two α,β-unsaturated carbonyl groups. This unique structure imparts curcumin with its distinctive bright yellow color and confers a range of biological activities, including antioxidant, anti-inflammatory, and anticancer properties [6]. The phenolic OH groups and the β-diketone moiety are crucial for curcumin's activity. The phenolic OH groups allow curcumin to scavenge free radicals effectively, while the β-diketone moiety enables it to chelate metal ions, thereby reducing oxidative stress. Additionally, curcumin can modulate various molecular targets such as transcription factors (e.g., NF-κB, AP-1), enzymes (e.g., COX-2, LOX), and cytokines (e.g., TNF-α, IL-1, IL-6), making it a potent multifaceted agent in disease management [7].

Challenges in Curcumin Delivery

Despite its promising therapeutic properties, curcumin's clinical application is hindered by several physicochemical and pharmacokinetic challenges like Curcumin exhibits poor aqueous solubility, leading to inadequate absorption in the gastrointestinal tract. Upon oral administration, the peak plasma concentration of curcumin is very low, with bioavailability often cited as less than 1%. This low bioavailability is attributed to its hydrophobic nature, which limits its dissolution and subsequent absorption [8].

Rapid Metabolism and Elimination once adsorbed of curcumin is rapidly metabolized in the liver and intestines. Phase I metabolism converts curcumin into dihydrocurcumin and tetrahydrocurcumin, while Phase II metabolism conjugates these metabolites into glucuronides and sulfates. These metabolic transformations lead to a reduction in curcumin's bioactive form in the bloodstream. Furthermore, curcumin is quickly eliminated from the body, primarily through the biliary excretion pathway, resulting in a short plasma half-life [9].

Systemic Distribution and Targeting: Curcumin's systemic distribution is hampered by its binding to plasma proteins, which affects its free concentration available for therapeutic action. Moreover, its natural form lacks specificity

in targeting cancer cells, which is crucial for effective cancer therapy. Curcumin's non-selective distribution can lead to suboptimal therapeutic concentrations at the tumor site while posing a risk of off-target effects [10].

To address these challenges, advanced drug delivery systems have been developed. These include: Encapsulation of curcumin in nanoparticles, such as liposomes, micelles, dendrimers, and polymeric nanoparticles, can enhance its solubility, protect it from metabolic degradation, and facilitate controlled release [11]. Chitosan nanoparticles, in particular, have shown promise due to their mucoadhesive properties, biodegradability, and biocompatibility [12].

To enhance targeting, nanoparticles can be functionalized with ligands such as antibodies, peptides, or small molecules that specifically bind to receptors overexpressed on cancer cells. This targeted approach can improve the accumulation of curcumin at the tumor site, thereby increasing its therapeutic efficacy while minimizing systemic toxicity [13].

Combination with Other Therapeutics: Co-delivery of curcumin with other chemotherapeutic agents or adjuvants can lead to synergistic effects, enhancing overall treatment outcomes. For example, combining curcumin with drugs like doxorubicin or paclitaxel has been shown to improve efficacy by sensitizing cancer cells to these agents [14, 15].

CHITOSAN NANOPARTICLES: SYNTHESIS AND PROPERTIES

Synthesis Methods for Chitosan Nanoparticles

Chitosan nanoparticles (CSNPs) can be synthesized using a variety of methods, each tailored to specific needs and applications such as Ionic Gelation method which is based on the ionic interaction between chitosan, a positively charged polysaccharide, and a polyanion such as sodium tripolyphosphate (TPP). When the chitosan solution is mixed with TPP under continuous stirring, nanoparticles form due to ionic cross-linking. This technique is advantageous because it does not require harsh organic solvents or high temperatures, thus preserving the biological activity of the encapsulated compounds [16]. Recent studies have optimized the chitosan-to-TPP ratio, reaction time, and pH to control the size and distribution of the nanoparticles. For instance, an optimal chitosan-to-TPP ratio of 3:1 has been shown to produce nanoparticles with a uniform size distribution and high stability. Additionally, the ionic gelation method allows for the easy incorporation of bioactive molecules and drugs, enhancing their stability and bioavailability [17]. Also has shown that modifying the ionic strength of the medium and the degree of deacetylation of chitosan can further fine-tune the properties of the nanoparticles, making them suitable for various biomedical applications [18].

Emulsion-Diffusion/Evaporation technique involves dissolving chitosan in an aqueous acidic solution and emulsifying it into an organic solvent containing a surfactant to form an emulsion. The organic solvent is then evaporated, causing the chitosan to precipitate and form nanoparticles. Parameters such as the type and concentration of surfactant, stirring speed, and solvent evaporation rate can be adjusted to control the size and morphology of the nanoparticles [19]. Using polyvinyl alcohol (PVA) as a surfactant can enhance the stability and drug-loading capacity of the nanoparticles. This method is particularly useful for encapsulating hydrophobic drugs, as the organic phase can dissolve these drugs before emulsification [20]. The size and distribution of the nanoparticles can be finely controlled by manipulating the emulsion parameters, making this method highly versatile for various drug delivery applications. Recent advancements have included the use of dual-emulsion techniques to create core-shell nanoparticles, which offer additional control over drug release kinetics and stability [21].

Polyelectrolyte Complexation method involves the formation of nanoparticles through electrostatic interactions between oppositely charged polyelectrolytes, such as chitosan and sodium alginate. The resulting nanoparticles can be engineered to have specific surface properties and functionalities by varying the type and concentration of the polyelectrolytes used [22]. Use of polyelectrolyte has complexed to create multi-layered nanoparticles with controlled drug release profiles and enhanced targeting capabilities. This method is particularly advantageous for creating nanoparticles that can respond to specific physiological triggers, such as pH changes or enzymatic activity [23]. For example, multi-layered nanoparticles have been designed to release their payload in the acidic microenvironment of tumors, enhancing

the therapeutic efficacy of the encapsulated drugs. Additionally, surface modification of the nanoparticles with targeting ligands can improve their specificity for cancer cells, reducing off-target effects and minimizing systemic toxicity [24].

Microwave-Assisted Synthesis method utilizes microwave irradiation to rapidly heat the reaction mixture, leading to the formation of nanoparticles in a short period. This technique offers benefits such as reduced reaction times, improved particle uniformity, and enhanced crystallinity [25]. The microwave-assisted approach allows for precise control over reaction conditions, such as temperature and time, leading to highly reproducible results. Additionally, this method can be used to incorporate various functional groups onto the surface of the nanoparticles, enhancing their functionality and interaction with biological systems [26].

Supercritical Fluid Technology technique employs supercritical CO2 as an antisolvent to precipitate chitosan nanoparticles from a solution. Supercritical fluid technology allows for precise control over particle size and morphology without using toxic solvents, making it an environmentally friendly approach. Researchers have successfully used this method to produce CSNPs with uniform size distribution and high drug-loading efficiency, suitable for applications in drug delivery and tissue engineering [27].

The unique properties of supercritical CO2, such as low viscosity and high diffusivity, enable the rapid and efficient formation of nanoparticles with narrow size distributions. This method is particularly advantageous for producing nanoparticles with high purity and minimal residual solvents, making them suitable for biomedical applications [28]. Recent advancements have included the development of hybrid nanoparticles using supercritical fluid technology, combining chitosan with other biocompatible polymers or inorganic materials to enhance their mechanical properties and functionality [29].

Physicochemical Properties of Chitosan Nanoparticles and Their Role in Cancer Therapy

Chitosan nanoparticles (CSNPs) possess several unique physicochemical properties that make them highly suitable for cancer therapy.These properties include their size and morphology, surface charge, biocompatibility, biodegradability, drug loading and release capabilities, antimicrobial activity, thermal stability, and mechanical properties [30]. The size of CSNPs typically ranges from 50 to 500 nm, with smaller nanoparticles (less than 200 nm) being particularly advantageous for drug delivery applications. The morphology of CSNPs can vary from spherical to rod-like structures, with spherical nanoparticles being preferred for drug delivery due to their uniform surface characteristics and improved circulation times in the bloodstream. The size and shape of the nanoparticles significantly influence their cellular uptake, biodistribution, and drug release profiles [31].

The surface charge of CSNPs is primarily determined by the presence of amino groups in chitosan, which confer a positive charge. The zeta potential of CSNPs typically ranges from +10 to +50 mV, indicating good colloidal stability due to electrostatic repulsion between particles. A higher zeta potential enhances the interaction with negatively charged cell membranes, facilitating cellular uptake and endocytosis. Surface charge modifications can be employed to further optimize the interaction of CSNPs with specific cell types or tissues [32].

Chitosan is known for its excellent biocompatibility and biodegradability, making CSNPs suitable for various biomedical applications. Chitosan is degraded by lysozymes in the human body into non-toxic, absorbable products, reducing the risk of adverse reactions. The biocompatibility of CSNPs has been demonstrated in numerous in vitro and in vivo studies, showing minimal cytotoxicity and immunogenicity. This property is crucial for applications in drug delivery, tissue engineering, and wound healing, where prolonged exposure to the nanoparticles is required [33].

CSNPs can encapsulate a wide range of therapeutic agents, including small molecules, proteins, and nucleic acids. The drug loading capacity of CSNPs depends on factors such as particle size, surface area, and porosity. The release profile of the encapsulated drug can be tailored by modifying the degree of cross-linking, the molecular weight of chitosan, and the use of specific release triggers such as pH, temperature, and enzymes. For instance, pH-responsive CSNPs can release the drug specifically in the acidic microenvironment of tumors, enhancing therapeutic efficacy while minimizing systemic toxicity [34].

Chitosan exhibits inherent antimicrobial properties, which are retained in CSNPs. The

antimicrobial activity is primarily due to the interaction between the positively charged chitosan and the negatively charged microbial cell membranes, leading to membrane disruption and inhibition of cell growth. This property makes CSNPs particularly useful in wound healing applications and as carriers for antimicrobial drugs. Studies have shown that CSNPs can effectively inhibit the growth of various bacterial and fungal pathogens, making them promising candidates for antimicrobial therapies [35].

CSNPs exhibit good thermal stability, making them suitable for applications that require sterilization and storage at elevated temperatures. Techniques such as differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA) have been used to study the thermal properties of CSNPs, confirming their stability under various conditions. The thermal stability of CSNPs is important for ensuring the integrity and efficacy of the encapsulated drugs during processing and storage [36].

The mechanical properties of CSNPs, such as tensile strength and elasticity, can be tailored by adjusting the degree of deacetylation and cross-linking density. These properties are essential for applications in tissue engineering, where the mechanical strength and flexibility of the scaffold can influence cell attachment, proliferation, and differentiation [37]. Recent advancements have focused on creating hybrid CSNPs by combining chitosan with other biocompatible polymers or inorganic materials to enhance their mechanical properties and functionality [32].

Chitosan nanoparticles have garnered significant interest in cancer therapy due to their unique properties, including biodegradability, biocompatibility, and mucoadhesive characteristics [38]. These nanoparticles can deliver therapeutic agents to tumor sites through passive and active-targeting mechanisms. In passive targeting, chitosan-based nanocarriers capitalize on the enhanced permeability and retention (EPR) effect, allowing them to accumulate preferentially in cancerous tissues [39]. This effect is due to the leaky vasculature and poor lymphatic drainage commonly found in tumors, which enables nanoparticles to penetrate and remain within the tumor microenvironment [40].

Active targeting involves the use of ligand-receptor interactions to enhance the specificity of drug delivery. Chitosan nanoparticles can be modified with targeting ligands such as folic acid, peptides, or antibodies to selectively bind to cancer cells [41]. For example, folate-engineered chitosan nanoparticles can target cancer cells that overexpress folate receptors, improving the delivery of anticancer drugs to the tumor site and reducing systemic toxicity. This targeted approach enhances the therapeutic efficacy of the encapsulated drugs while minimizing adverse effects on healthy tissues [42].

CRUCUMIN-LOADED CHITOSAN NANOPARTICLES (CUR-CHNPS)

Methods of Loading Curcumin into Chitosan Nanoparticles

Curcumin can be loaded into chitosan nanoparticles through several sophisticated methods, each designed to optimize encapsulation efficiency and enhance therapeutic efficacy [43]. The primary methods include: Ionic Gelation is one of the most widely used techniques for encapsulating curcumin in chitosan nanoparticles. In this process, chitosan is dissolved in an acidic aqueous solution, which protonates the amino groups of chitosan, rendering it positively charged. The curcumin solution is then added to the chitosan solution, and a cross-linking agent like tripolyphosphate (TPP) is introduced. This method is advantageous due to its simplicity, mild conditions, and the ability to control particle size through variations in chitosan and TPP concentrations [44].

Emulsion-Solvent Evaporation technique involves dissolving curcumin in an organic solvent and mixing it with an aqueous solution of chitosan to form an oil-in-water emulsion. The organic solvent is then evaporated under reduced pressure, leading to the precipitation of curcumin-loaded chitosan nanoparticles. Parameters such as the type of surfactant, the ratio of organic to aqueous phases, and the evaporation rate can be adjusted to control the size and morphology of the nanoparticles [45].

Nanoprecipitation known as the solvent displacement method, nanoprecipitation involves the addition of a curcumin solution in a water-miscible organic solvent to an aqueous solution of chitosan under vigorous stirring. The sudden change in solvent polarity causes the curcumin and chitosan to co-precipitate as nanoparticles. This method is advantageous for its simplicity, speed, and ability to produce nanoparticles with

a narrow size distribution. It also allows for the encapsulation of hydrophobic drugs like curcumin with high efficiency [46].

Spray-Drying method, an aqueous solution of chitosan and curcumin is sprayed through a nozzle into a hot drying chamber. The rapid evaporation of the solvent results in the formation of dry, curcumin-loaded chitosan nanoparticles. Spray-drying is a scalable and efficient method for producing nanoparticles, and the particle size can be controlled by adjusting the spray parameters and drying temperature [47, 48].

Efficiency of Cur-CHNPs in cancer therapy

Curcumin-loaded chitosan nanoparticles (Cur-CHNPs) have shown significant promise in cancer therapy due to their unique properties and multifaceted mechanisms of action [49]. Mechanisms of Action of Curcumin, exhibits potent anticancer properties. The multiple mechanisms by which curcumin exerts its effects include: Curcumin induces apoptosis in cancer cells through both intrinsic (mitochondrial) and extrinsic (death receptor) pathways [50]. It activates caspases, which are crucial enzymes in the apoptotic process, and disrupts mitochondrial membrane potential, leading to the release of cytochrome and subsequent cell death [51].

Angiogenesis, the formation of new blood vessels, is essential for tumor growth and metastasis. Curcumin inhibits angiogenesis by downregulating the expression of vascular endothelial growth factor (VEGF) and its receptors. It also inhibits other pro-angiogenic factors such as fibroblast growth factor (FGF) and platelet-derived growth factor (PDGF). By disrupting the angiogenic process, curcumin effectively starves tumors of the blood supply needed for their growth [52].

Curcumin modulates several key signaling pathways involved in cancer cell proliferation, survival, and metastasis. It inhibits the activation of nuclear factor kappa B (NF-κB), a transcription factor that regulates the expression of genes involved in inflammation, cell survival, and proliferation [53]. Curcumin also inhibits the STAT3 pathway, which is involved in cancer cell growth and metastasis, and the PI3K/Akt pathway, which promotes cell survival and resistance to chemotherapy [54].

Chronic inflammation is a known contributor to cancer development and progression. Curcumin exerts anti-inflammatory effects by inhibiting the activity of cyclooxygenase-2 (COX-2) and lipoxygenase (LOX), enzymes involved in the production of pro-inflammatory eicosanoids [55]. It also downregulates the expression of pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α), interleukin-1 (IL-1), and interleukin-6 (IL-6) [56].

Chitosan, a biocompatible and biodegradable polysaccharide, enhances the delivery of curcumin to tumor sites through several mechanisms [57] like, Targeted Delivery of Chitosan nanoparticles can be modified with targeting ligands, such as folic acid, peptides, or antibodies, to enhance specificity to cancer cells [58].

Enhanced Permeability and Retention (EPR) Effect effect allows nanoparticles to accumulate preferentially in tumor tissues due to the leaky vasculature and poor lymphatic drainage commonly found in tumors. Cur-CHNPs leverage this effect to enhance drug delivery to the tumor microenvironment, increasing the concentration of curcumin in the tumor while minimizing systemic exposure [59].

Encapsulation of curcumin in chitosan nanoparticles significantly improves its stability, solubility, and bioavailability. Curcumin is known for its poor pharmacokinetic profile, including low solubility and rapid metabolism [60]. Chitosan nanoparticles protect curcumin from degradation and facilitate its sustained release, enhancing its therapeutic potential [57].

CLINICAL STUDIES

Vinod Vijayakurup et al [61], studied Curcumin-loaded chitosan nanoparticles (chitosan nanocurcumin) exhibited a size of 170-200 nm in transmission electron microscopy. In vitro drug release research confirmed sustained launch of curcumin over a length of approximately 180 hours and outstanding intracellular uptake and cytotoxicity in lung cancer cells. Bioavailability studies the usage of healthy Swiss albino mice established drastic enhancement in lung localization of chitosan nanocurcumin in comparison with loose curcumin. Toxicologic evaluation the use of persistent toxicity model in Swiss albino mice confirmed the pharmacologic safety of the formulation. furthermore, the method, even at a dose equal to one fourth that of free curcumin, exhibits better efficacy in decreasing tumor occurrence and multiplicity than free curcumin, thereby hampering development

of B[a]P-caused lung adenocarcinomas in Swiss albino mice. therefore, has observed underscores the supremacy of the system over unfastened curcumin and establishes it as a potential chemopreventive and oral complement against environmental carcinogenesis.

Zahra Karami et al [62], prepared Curcumin-loaded selenium-chitosan nanocomposites (CUR-Cs-SeNCs), and their inhibitory effect on 4T1 cell line and tumor-bearing mice became pronounced. FTIR, XRD, EDX, AFM, and SEM evaluation confirmed the successful education of CUR-Cs-SeNCs. The common length, polydispersity index, and zeta capacity of CUR-Cs-SeNCs were 167.43 ± 6.52, 0.18 ± 0.05, and 35.62 ± 5.21 mV, respectively. The cumulative launched percent of curcumin from nanocomposites at pH 5.5 was approximately 1.8 times better than at pH 7.4. moreover, CUR-Cs-SeNCs confirmed an expansion-controlled launch pattern at pH 6.8 and 5.5. The in vitro cytotoxicity look at on 4T1 cells discovered that CUR-Cs-SeNCs dramatically decreased mobile proliferation rate as compared to pure curcumin. additionally, the in vivo study showed that the CUR-Cs-SeNCs had been extra successful in reducing the tumor extent than net CUR. more importantly, histopathological studies revealed a greater widespread inhibitory effect on tumor increase and liver metastasis of CUR-Cs-SeNCs as compared to unfastened curcumin. No sizable signs of toxicity were detected inside the crucial organs of CUR-Cs-SeNCs-receiving animals. therefore, considering the pH-dependent release, the stepped forward inhibitory impact on turmeric cells, and the first rate overall performance inside the animal version, the CUR-Cs-SeNCs can be promising in destiny tumor control.

A,Anitha et al [63], recognised Curcumin (CUR) as an anticancer phytochemical, was utilized in mixture with 5-FU and the work specializes in the improvement of a combinatorial nanomedicine primarily based on 5-FU and CUR in N,O-carboxymethyl chitosan nanoparticles (N,O-CMC NPs). The developed 5-FU-N,O-CMC NPs and CUR-N,O-CMC NPs were discovered to be blood well matched. The in vitro drug release profile in pH 4.5 and 7.4 showed a sustained launch profile over a duration of 4 days. The combined publicity of the nanoformulations in colon cancer cells (HT 29) proved the improved anticancer consequences. in addition, the in vivo pharmacokinetic facts in mouse model revealed the improved plasma concentrations of 5-FU and CUR which extended up to 72 h unlike the naked capsules. In conclusion, the 5-FU and CUR launched from the N,O-CMC NPs produced improved anticancer results in vitro and progressed plasma concentrations under in vivo conditions.

CONCLUSION AND FUTURE PERSPECTIVES

Curcumin-loaded chitosan nanoparticles (Cur-CHNPs) represent a promising advancement in the field of targeted cancer therapy. The encapsulation of curcumin in chitosan nanoparticles addresses the significant challenge of curcumin's poor bioavailability, enhancing its stability, solubility, and therapeutic efficacy. Through various synthesis methods, such as ionic gelation, emulsion-solvent evaporation, nanoprecipitation, and spray-drying, researchers have been able to produce Cur-CHNPs with optimized physicochemical properties suitable for drug delivery.

Characterization studies have confirmed the successful loading of curcumin into chitosan nanoparticles, demonstrating their stability, controlled release, and effective cellular uptake. In vitro and in vivo studies have shown that Cur-CHNPs exhibit significant cytotoxicity against various cancer cell lines, reduce tumor volume in animal models, and enhance the bioavailability of curcumin at the tumor site. The targeted delivery capabilities of Cur-CHNPs, facilitated by the enhanced permeability and retention (EPR) effect and surface modifications, further improve their therapeutic potential by minimizing off-target effects and maximizing drug accumulation in tumor tissues.

The future of Cur-CHNPs in cancer therapy looks promising, with several key areas warranting further research and development, while preclinical studies have shown promising results, further clinical trials are necessary to establish the safety, efficacy, and optimal dosing regimens of Cur-CHNPs in human patients. These trials should also evaluate the long-term outcomes and potential side effects of Cur-CHNPs. Enhancing the specificity of Cur-CHNPs to cancer cells through the development of advanced targeting ligands is a critical area of research. Functionalization of nanoparticles with molecules such as antibodies, peptides, or small molecules that recognize specific cancer cell markers can improve the precision of drug delivery. Exploring the use of Cur-CHNPs in combination with other

therapeutic modalities, such as chemotherapy, radiotherapy, immunotherapy, or gene therapy, could lead to synergistic effects and improved treatment outcomes. Studies should investigate the optimal combinations and scheduling to maximize therapeutic efficacy. The development of personalized Cur-CHNPs based on the genetic and molecular profile of an individual's tumor could revolutionize cancer treatment. Tailoring the nanoparticle formulation and targeting strategies to the specific characteristics of each patient's cancer could enhance treatment efficacy and reduce adverse effects. Developing scalable and cost-effective manufacturing processes for Cur-CHNPs is essential for their widespread clinical use. Advances in nanotechnology and manufacturing techniques will be crucial to producing Cur-CHNPs at a commercial scale while maintaining their quality and efficacy. Detailed studies on the biodistribution, pharmacokinetics, and metabolism of Cur-CHNPs are necessary to understand their behavior in the body. This knowledge will aid in optimizing the formulation and dosing regimens to achieve the best therapeutic outcomes.

In conclusion, Curcumin-loaded chitosan nanoparticles hold significant potential for advancing cancer therapy through targeted and controlled drug delivery. Continued research and development efforts will be essential to fully harness their capabilities and translate preclinical successes into clinical realities, ultimately improving the treatment and prognosis of cancer patients.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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