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RESEARCH PAPER

Review of Advancements in Liver Cancer Treatment: The Role of Artemisinin-Loaded Lipid Nanoparticles

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ABSTRACT

Liver cancer, often hepatocellular carcinoma (HCC), is a leading cause of cancer-related deaths worldwide. conventional therapies, such as surgical treatment, radiation, and chemotherapy, regularly fall short because of systemic toxicity, drug resistance, and limited efficacy. Artemisinin, a well-known antimalarial drug, has validated huge anticancer homes. latest advancements in nanotechnology have facilitated the improvement of lipid nanoparticles as efficient drug transport systems, improving the therapeutic capability of artemisinin in liver cancer remedy. This review ambitions to provide a comprehensive evaluate of the advancements in liver cancer remedy, focusing on the position of artemisinin-loaded lipid nanoparticles. It explores the mechanisms of motion of artemisinin, the advantages of lipid nanoparticles in drug delivery, and the synergistic consequences observed in preclinical and medical studies. The review also discusses the modern challenges and future perspectives in leveraging this innovative approach for effective liver cancer therapy. This paper highlights Artemisinin-loaded lipid nanoparticles constitute a promising method for liver cancer treatment. by exploiting the particular properties of each artemisinin and lipid nanoparticles, this approach offers superior tumor targeting, improved drug bioavailability, and reduced systemic toxicity. persisted studies and medical validation are critical to absolutely understand the ability of this novel healing strategy, doubtlessly remodeling the panorama of liver cancer treatment and enhancing patient effects.

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INTRODUCTION

Liver cancers, especially hepatocellular carcinoma (HCC), stays one of the most formidable worldwide fitness demanding situations, contributing extensively to cancer-related mortality. according to the (WHO), liver cancer accounted for nearly 830,000 deaths global in 2020, emphasizing the urgent need for effective therapeutic strategies [1]. conventional treatments for liver cancer include surgical resection, liver transplantation, nearby ablative therapies, chemotherapy, and radiation remedy. while these strategies can be effective in positive situations, they regularly fall short because of numerous limitations, which includes systemic toxicity, development of drug resistance, and limited efficacy in advanced levels of the disorder [2]. Chemotherapy, a cornerstone in the control of systemic malignancies, relies heavily on cytotoxic agents that indiscriminately target hastily dividing cells. although this method can be powerful towards cancer cells, it also influences healthful tissues, leading to huge adverse results including myelosuppression, mucositis, and nephrotoxicity [3]. In recent years, nanotechnology has emerged as a promising field for enhancing cancer treatment through enhancing the delivery and specificity of therapeutic agents. Nanoparticles, because of their small length and modifiable surface residences, can be engineered to enhance drug solubility, balance, and bioavailability [4]. A few of the numerous sorts of nanoparticles, lipid nanoparticles have garnered significant interest because of their biocompatibility and capability to encapsulate each hydrophobic and hydrophilic drugs. these lipid-based carriers can facilitate the targeted delivery of chemotherapeutic agents to tumor sites, thereby reducing systemic toxicity and improving therapeutic consequences [5]. One innovative technique includes the usage of artemisinin, a drug traditionally used to treat malaria, which has established amazing anticancer properties. Artemisinin and its derivatives had been shown to exert cytotoxic outcomes on cancer cells through numerous mechanisms, which includes the technology of reactive oxygen species (ROS) and the induction of apoptosis [6]. However, the clinical application of artemisinin in most cancers remedy has been limited by its poor solubility and stability. to overcome these challenges, researchers have explored the encapsulation of artemisinin in lipid nanoparticles, aiming to enhance its delivery and efficacy in cancer treatment [7]. Artemisinin-loaded lipid nanoparticles (ALNs) represent a promising approach for liver cancer remedy, leveraging the benefits of each artemisinin and lipid nanoparticle-primarily based delivery systems [8]. These nanoparticles are designed to take advantage of the precise characteristics of the tumor microenvironment (TME), inclusive of the marginally acidic extracellular pH (6.5–7.0) or even decrease pH degrees within intracellular cubicles (45–5.5), to achieve controlled drug release [9]. The dual pH-sensitive nature of these structures ensures that artemisinin is released primarily at the tumor site, thereby sparing healthful tissues and minimizing systemic side effects. moreover, using concentrated on ligands on the surface of the nanoparticles can enhance the specificity and uptake of artemisinin by using cancer cells, in addition enhancing therapeutic effects [10].

The goal of this review is to provide a

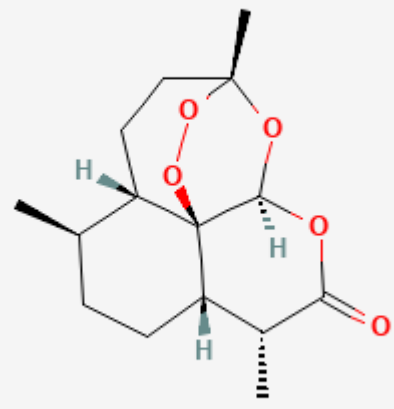

Fig. 1. Chemical structure of Artimisinin

comprehensive overview of the improvements in liver cancer remedy, with a specific recognition at the role of artemisinin-loaded lipid nanoparticles. This review will explore the mechanisms of action of artemisinin, the benefits of lipid nanoparticles in drug shipping, and the synergistic outcomes observed in preclinical and clinical studies. additionally, it will discuss the current challenges and future perspectives in leveraging this modern approach for effective liver cancer remedy. the novelty of this review lies in its comprehensive evaluation of the twin benefits of artemisinin and lipid nanoparticles, highlighting their capability to transform liver cancer treatment by improving drug delivery, improving therapeutic outcomes, and reducing systemic toxicity.

ARTEMISININ: A POTENTIAL ANTICANCER AGENT

Historical Background

Artemisinin, is known with $C_{15}H_{22}O_5$ molecular formula that is a sesquiterpene lactone derived from Artemisia annua (sweet wormwood), has its origins in traditional Chinese medicine (Fig. 1 show the chemical structure of ART). Its discovery for malaria treatment was propelled by the Project 523 initiative during the 1970s in China, aimed at addressing chloroquine-resistant malaria [11]. Tu Youyou's groundbreaking work on isolating artemisinin earned her the 2015 Nobel Prize in Physiology or Medicine, marking the compound as a globally recognized therapeutic agent [12]. Beyond its antimalarial efficacy, artemisinin's potential as an anticancer agent began gaining attention in the late 1990s [13]. This interest was initially spurred by its ability to generate reactive oxygen species (ROS) in the presence of high intracellular iron concentrations. Cancer cells often exhibit dysregulated iron metabolism due to overexpression of transferrin receptors, making them particularly vulnerable to artemisinin's iron-dependent cytotoxic effects [14]. Further investigations revealed artemisinin's broad-spectrum anticancer activity against various malignancies, including liver cancer. Hepatocellular carcinoma (HCC), one of the most prevalent and lethal liver cancers worldwide, is characterized by high oxidative stress and metabolic dysregulation [15]. These characteristics align with artemisinin's mechanisms of action, positioning it as a promising therapeutic candidate. However, challenges such as poor water solubility, limited bioavailability, and rapid metabolism in vivo have spurred the development of artemisinin-loaded lipid nanoparticles (ALNs) to enhance its pharmacokinetic and pharmacodynamic profiles [16]. The incorporation of artemisinin into lipid-based delivery systems has shown significant potential to overcome these limitations [17]. Lipid nanoparticles not only improve drug solubility but also enable targeted delivery, sustained release, and reduced systemic toxicity. These advancements represent a critical step toward translating artemisinin-based therapies into clinical applications for liver cancer treatment [18].

Mechanisms of Action

Artemisinin's anticancer properties are rooted in its unique chemical structure, particularly the endoperoxide bridge, which is critical for its bioactivity. The mechanism of action primarily involves the generation of reactive oxygen species (ROS) upon interaction with intracellular iron [19]. Cancer cells, including those in hepatocellular carcinoma (HCC), demonstrate aberrant iron metabolism characterized by elevated transferrin receptor expression and iron accumulation. This dependency renders them more susceptible to ROS-induced oxidative damage [20]. Upon activation by iron, artemisinin generates cytotoxic free radicals that target cellular macromolecules, leading to apoptosis and ferroptosis [21]. Studies in HCC have demonstrated that artemisinin induces mitochondrial dysfunction, disrupting cellular respiration and energy production. This is further compounded by its ability to modulate key signaling pathways, including the PI3K/AKT/mTOR axis, thereby inhibiting cell proliferation and enhancing apoptosis [22]. Another critical mechanism involves the modulation of angiogenesis. Artemisinin has been shown to suppress vascular endothelial growth factor (VEGF) signaling, a pathway pivotal for tumor angiogenesis and metastasis [23]. This is particularly significant in liver cancer, which relies heavily on neo-angiogenesis for growth and dissemination. Additionally, artemisinin enhances the efficacy of conventional therapies by sensitizing cancer cells to chemotherapeutic agents and radiotherapy, potentially reducing resistance [24]. Emerging evidence highlights the role of artemisinin in modulating the tumor microenvironment (TME) [25]. It reduces inflammatory cytokine production and reprograms immune cells, such as macrophages, toward an

antitumor phenotype. These immune-modulatory effects, combined with its direct cytotoxicity, amplify its anticancer potential [26]. To address limitations in its pharmacokinetics, artemisinin-loaded lipid nanoparticles (ALNs) have been developed to enhance its therapeutic efficacy [27]. These nanoparticles improve drug stability, allow controlled release, and facilitate targeted delivery to the liver, maximizing artemisinin's anticancer activity while minimizing off-target effects. Preliminary studies have shown that ALNs exhibit superior ROS generation, tumor penetration, and therapeutic outcomes in HCC models compared to free artemisinin [17].

LIPID NANOPARTICLES AS DRUG DELIVERY SYSTEMS

Basics of Lipid Nanoparticles

Lipid nanoparticles (LNPs) are a class of nanoscale drug delivery systems engineered from lipids that are biocompatible and biodegradable. These systems include two principal types, solid lipid nanoparticles (SLNs), composed entirely of solid lipids, and nanostructured lipid carriers (NLCs), which are hybrids of solid and liquid lipids [28]. The inclusion of liquid lipids in NLCs reduces crystallinity, resulting in higher drug loading efficiency and controlled drug release profiles [29]. LNPs are typically manufactured using advanced methods such as high-pressure homogenization, microemulsion techniques, or solvent evaporation [30]. These processes produce particles within the nanometer range (50–300 nm), which is crucial for enhancing drug solubility, stability, and bioavailability. This nanoscale size ensures efficient tissue penetration and uptake by cells through endocytosis, enabling LNPs to target specific sites, such as the liver, with high precision [31]. The functional architecture of LNPs includes a hydrophobic lipid core, which serves as a reservoir for poorly water-soluble drugs, surrounded by a stabilizing monolayer of surfactants or polymers [27]. The outer surface can also be functionalized with ligands, antibodies, or peptides to target specific cellular receptors, enhancing selectivity for cancerous tissues [8]. LNPs are particularly effective for delivering artemisinin, whose clinical application has been limited by poor aqueous solubility, rapid metabolism, and a short half-life. Encapsulation within LNPs protects artemisinin from degradation, prolongs systemic circulation, and allows for sustained drug release [32]. This targeted delivery significantly enhances the pharmacological efficacy of artemisinin while minimizing off-target toxicities, making LNPs a critical advancement for hepatocellular carcinoma (HCC) therapy [24].

In liver cancer treatment, LNPs exploit the enhanced permeability and retention (EPR) effect observed in tumors [33]. This passive targeting mechanism allows LNPs to accumulate selectively in tumor tissue, a feature further augmented by active targeting strategies that interact with receptors overexpressed in HCC, such as transferrin receptors [34].

Advantages in Cancer Therapy

Lipid nanoparticles (LNPs) represent a transformative approach in cancer therapy due to their ability to address the challenges of conventional drug delivery systems. Their nanoscale size enables selective tumor targeting through the enhanced permeability and retention (EPR) effect, wherein nanoparticles accumulate preferentially in tumor tissues due to leaky vasculature and poor lymphatic drainage [33]. This passive targeting mechanism is particularly effective for hepatocellular carcinoma (HCC), where localized delivery is critical for therapeutic efficacy [27]. One of the primary advantages of LNPs is their ability to encapsulate lipophilic and hydrophilic drugs, enhancing the solubility and stability of chemotherapeutic agents [35]. Artemisinin, a hydrophobic compound with limited clinical utility due to its rapid clearance and poor bioavailability, benefits significantly from LNP encapsulation. The lipid matrix stabilizes the drug, reduces degradation, and enables sustained release, maintaining therapeutic drug levels over extended periods [36]. LNPs also allow for controlled drug release and reduced systemic toxicity. By tailoring the lipid composition and particle size, the release profile of encapsulated drugs can be optimized to ensure maximal efficacy with minimal side effects [8]. Functionalized LNPs, modified with targeting ligands such as transferrin or folic acid, further enhance selectivity for HCC cells, reducing off-target effects on healthy tissues [37]. In addition to improving drug delivery, LNPs facilitate combination therapies. Co-encapsulation of artemisinin with chemotherapeutics or immune checkpoint inhibitors in a single nanoparticle can synergistically target multiple cancer pathways [32]. For instance, the ROS-generating properties

of artemisinin, combined with the cytotoxic effects of doxorubicin, have shown enhanced tumor suppression in preclinical models of HCC [38]. Furthermore, LNPs are biocompatible and biodegradable, minimizing long-term toxicity and immunogenicity. Their ability to penetrate the tumor microenvironment and overcome drug resistance mechanisms makes them a versatile platform for liver cancer therapy [39]. Preclinical studies have demonstrated that artemisinin-loaded LNPs achieve superior tumor inhibition and reduced metastasis compared to free drugs, underscoring their potential in clinical applications [34].

EFFICACY OF ARTEMISININ-LOADED LIPID NANOPARTICLES

Comparison with Conventional Treatments

Artemisinin's poor aqueous solubility and rapid degradation pose significant challenges for its clinical use. Encapsulation within lipid nanoparticles addresses these issues by significantly improving solubility and stability. The lipid matrix of the nanoparticles provides a protective environment, preventing premature hydrolytic and enzymatic degradation of artemisinin. This leads to prolonged retention and sustained therapeutic action in the biological system [40]. Lipid nanoparticles are designed to exploit the Enhanced Permeability and Retention (EPR) effect, which is a phenomenon where nanoparticles accumulate preferentially in tumor tissues due to the aberrant and leaky vasculature. This passive targeting mechanism significantly enhances the accumulation of artemisinin at the tumor site, improving therapeutic efficacy and minimizing systemic exposure and associated side effects. Additionally, surface modification of lipid nanoparticles with targeting ligands such as antibodies or peptides can further enhance specificity towards cancer cells, ensuring that the therapeutic agent is delivered precisely to the desired location [41]. Lipid nanoparticles can be engineered to provide a controlled and sustained release of artemisinin, which is achieved through careful selection and design of the lipid matrix. Techniques such as optimizing lipid composition, particle size, and encapsulation methods are employed to achieve desired release kinetics. This ensures a steady and prolonged release of artemisinin, maintaining therapeutic drug levels over extended periods and reducing the frequency of administration. Moreover, the controlled release profile helps in maintaining a consistent cytotoxic effect on cancer cells, enhancing therapeutic outcomes [42]. Encapsulation of artemisinin in lipid nanoparticles significantly reduces its systemic toxicity. By facilitating targeted delivery of the drug specifically to the tumor site, exposure of healthy tissues to the cytotoxic effects of artemisinin is minimized. This targeted approach mitigates common adverse effects associated with conventional chemotherapy, such as gastrointestinal disturbances, hepatotoxicity, and myelosuppression. Additionally, the use of biocompatible and biodegradable lipids in the formulation of nanoparticles further contributes to reducing toxicity [43]. The lipid components of lipid nanoparticles themselves can exert additional therapeutic effects, enhancing the overall anticancer efficacy of artemisinin. For instance, the lipid matrix can facilitate the generation of reactive oxygen species (ROS), which induce apoptosis and inhibit the proliferation of cancer cells. Furthermore, the combination of artemisinin with lipids can modulate various signaling pathways involved in cancer progression, exerting a synergistic anticancer effect. This synergy is particularly beneficial in overcoming drug resistance and enhancing the therapeutic index of artemisinin [44].

Synthesis and Characterization

The synthesis of artemisinin-loaded LNPs involves advanced techniques that ensure particle uniformity, high drug encapsulation efficiency, and stability. Common methods include, High-Pressure Homogenization (HPH): Artemisinin and lipids are dissolved in a compatible organic solvent, followed by homogenization under high shear forces. This technique produces stable nanoparticles with a narrow size distribution, essential for reproducibility in clinical applications [45, 46].

Solvent Evaporation: Artemisinin and lipid components are dissolved in a volatile solvent, emulsified in an aqueous surfactant solution, and subjected to solvent removal under reduced pressure. This method is efficient for incorporating hydrophobic drugs like artemisinin into the lipid matrix [47].

Microemulsion Techniques: Based on temperature-induced phase transitions, microemulsions are formed by mixing lipids, surfactants, and water in optimized ratios. This

method is advantageous for producing particles with controlled sizes and high encapsulation efficiency [33].

Key parameters optimized during synthesis include lipid-to-drug ratios, type of surfactant (e.g., Tween 80 or lecithin), and processing conditions like temperature and pressure [37]. The encapsulation efficiency (EE) of artemisinin typically exceeds 85% in well-optimized formulations, with drug loading capacities adjusted to maintain therapeutic levels over prolonged periods [48].

Particle Size and Distribution is dynamic light scattering (DLS) measures the hydrodynamic diameter of LNPs, which is ideally maintained between 50–200 nm for tumor targeting. Smaller sizes improve tissue penetration, while larger particles risk rapid clearance by the reticuloendothelial system (RES) [49]. Zeta potential analysis determines surface charge, which influences colloidal stability and cellular uptake. A value of ±30 mV or higher ensures stability in biological environments [50].

Morphology: Transmission electron microscopy (TEM) or scanning electron microscopy (SEM) provides detailed images of nanoparticle structure and confirms spherical shape [8]. Encapsulation Efficiency and Drug Loading: High-performance liquid chromatography (HPLC) quantifies the amount of artemisinin encapsulated relative to the initial drug input, optimizing formulations for maximum efficacy [51].

COMBINING ARTEMISININ WITH LIPID NANOPARTICLES IN LIVER CANCER

Mechanism and action

Artemisinin-loaded lipid nanoparticles (ALNs) offer a promising approach for liver cancer therapy. This combination utilizes the unique properties of both artemisinin and lipid-based delivery systems to enhance therapeutic efficacy while minimizing systemic side effects [52]. Artemisinin suffers from poor aqueous solubility and rapid degradation under physiological conditions. Encapsulation within lipid nanoparticles significantly improves its solubility and stability. The lipid matrix provides a protective environment, preventing hydrolytic and enzymatic degradation. This enhancement is crucial for maintaining therapeutic levels of artemisinin over extended periods [53]. Lipid nanoparticles exploit the Enhanced Permeability and Retention (EPR) effect, which allows nanoparticles to accumulate preferentially in tumor tissues due to their leaky vasculature. This passive targeting mechanism significantly enhances the concentration of artemisinin at the tumor site. The EPR effect ensures that more of the drug reaches the cancerous cells, improving therapeutic efficacy and reducing systemic exposure [41]. The tumor microenvironment (TME) is characterized by a slightly acidic extracellular pH (6.5–7.0) and even lower pH levels within intracellular compartments (4.5–5.5). ALNs are designed to be pH-sensitive, ensuring that artemisinin is released primarily at the tumor site. This dual pH-sensitive nature of ALNs exploits the acidic conditions of the TME to trigger controlled drug release, sparing healthy tissues and minimizing systemic side effects [43]. The surface of lipid nanoparticles can be modified with targeting ligands, such as antibodies or peptides, which enhance the specificity and uptake of artemisinin by cancer cells. This targeting approach ensures that the drug is delivered precisely to the desired location, further improving therapeutic outcomes. The ligands bind to specific receptors overexpressed on cancer cells, facilitating receptor-mediated endocytosis and enhancing cellular uptake [54]. The lipid components of ALNs can exert additional therapeutic effects that enhance the overall anticancer efficacy of artemisinin. For example, the lipid matrix can facilitate the generation of reactive oxygen species (ROS), which induce apoptosis and inhibit cancer cell proliferation. The combination of artemisinin with lipids can also modulate signaling pathways involved in cancer progression, exerting a synergistic anticancer effect [44]. The synergistic effects further enhance the efficacy of this novel delivery system, making ALNs a promising strategy for the treatment of liver cancer.

Clinical studies

Qing Wang et al [55], considering the critical position of heme in the precise parasite-killing impact of ART, designed a liposomal nanostructure self-assembled from hemin-lipid (Hemesome) to co-deliver ART and hemin for cancer therapy. The synergistic chemotherapeutic and immunotherapeutic effects of hemin and ART had been demonstrated each in vitro and in vivo. The liposome-like structure changed into noticeably stable within the blood move and gastrointestinal tract environment, but dissociated within the tumor cellular environment. The folic

acid (FA) amendment no longer simplest elevated their performance for shipping throughout the epithelium, but additionally improved their tumor accumulation. In mouse models, following oral administration of FA-Hemesome-ART nanoparticles (5 mg kg−1 ART in general) every different day and intraperitoneal injection with a programmed death-ligand 1 antibody (aPD-L1, 70 μg in step with mouse in total), MC38 tumors have been completely inhibited within 30 days. The cured mice remained tumor-unfastened 30 days after rechallenging them with another inoculation of MC38 cells because of the sturdy immune memory effect.

Praveesh Valissery et al [56], improved the aqueous segment solubility of artemisinin with the aid of encapsulating it in nanocarriers based totally on the polymer polycaprolactone (ART-PCL) and lipid-based totally huge Unilamellar Vesicles (art-LIPO) respectively. each nanoformulations exhibit in vitro parasite killing hobby in opposition to Plasmodium falciparum with the ART-LIPO acting at comparable efficacy to the manipulate drug solubilized in ethanol. These water-soluble formulations confirmed powerful in vivo antimalarial activity as well in the mouse model of malaria at equivalent doses of the parent drug. moreover, the artemisinin-PCL nanoformulation utilized in mixture with both pyrimethamine or chloroquine elevated the survival of the Plasmodium berghei infected mice for more than 34 days and effectively cured the mice of the infection. Is highlighted the capacity for polymer and liposome-based nanocarriers in improving not simplest the aqueous phase solubility of artemisinin however additionally concomitantly retaining its therapeutic efficacy in vivo as well.

Bin Zheng et al [57], conducted experiment for reducing the first-pass hepatic effect via intestinal lymphatic transport is a powerful way to increase the oral absorption of medication. 2-Monoacylglycerol (2-magazine) as a number one digestive made from nutritional lipids triglyceride, can be assembled in chylomicrons and then transported from the intestine into the lymphatic system. advocate a biomimetic approach and stated a 2-mag mimetic nanocarrier to goal the intestinal lymphatic gadget through the lipid absorption pathway and enhance oral bioavailability. the 2-mag mimetic liposomes had been designed by using covalently bonding serinol (SER) on the surface of liposomes named SER-LPs to simulate the structure of 2-mag. Dihydroartemisinin (DHA) was selected because the model drug because of its disadvantages along with poor solubility and high first-pass impact. The endocytosis and exocytosis mechanisms have been investigated in Caco-2 cells and Caco-2 cell monolayers. The capability of intestinal lymphatic transport was evaluated by using ex vivo biodistribution and in vivo pharmacokinetic experiments. DHA loaded SER-LPs (SER-LPs-DHA) had a particle length of 70 nm and a applicable entrapment performance of 93%. SER-LPs showed sustained release for DHA in the simulated gastrointestinal surroundings. In vitro cell studies confirmed that the cellular uptake of SER-LPs frequently relied on the caveolae- instead of clathrin-mediated endocytosis pathway and favored to combine into the chylomicron meeting technique via the endoplasmic reticulum/Golgi apparatus direction. After oral management, SER-LPs efficiently promoted drug accumulation in mesenteric lymphatic nodes. The oral bioavailability of DHA from SER-LPs changed into 10.40-fold and 1.17-fold larger than that of free DHA and unmodified liposomes on the identical dose, respectively. SER-LPs progressed oral bioavailability via efficient intestinal lymphatic transport. these findings of the current study provide a good alternative method for oral transport of medication with high first-pass hepatic metabolism.

CONCLUSION

The integration of artemisinin into lipid nanoparticles represents a transformative advancement in liver cancer therapy. By leveraging the enhanced solubility and stability provided by lipid matrices, these nanoparticles ensure that artemisinin remains effective and is delivered directly to the tumor site. The exploitation of the Enhanced Permeability and Retention (EPR) effect allows for targeted delivery, significantly improving therapeutic efficacy while minimizing systemic exposure and side effects. The dual pH-sensitive release mechanism of ALNs is particularly advantageous, as it ensures that artemisinin is released predominantly in the slightly acidic tumor microenvironment, thereby sparing healthy tissues. The use of targeting ligands on the nanoparticle surface further enhances the specificity and uptake of artemisinin by cancer cells, maximizing the therapeutic impact. Moreover, the lipid components themselves

can exert synergistic effects, such as facilitating the generation of reactive oxygen species (ROS) and modulating signaling pathways involved in cancer progression. This combination not only improves the efficacy of artemisinin but also helps in overcoming drug resistance.Overall, the advancements in the design and application of artemisinin-loaded lipid nanoparticles highlight their potential as a potent and promising strategy for liver cancer treatment. These innovations pave the way for more effective and safer therapeutic options, contributing significantly to the ongoing efforts to combat liver cancer.

CONFLICT OF INTEREST

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

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