Review

# Advances of nano-targeted drug delivery systems in traditional Chinese medicine anticancer therapy

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**Abstract:** Cancer has now become the second leading cause of mortality, following cardiovascular and cerebrovascular diseases. Traditional Chinese medicine (TCM) has emerged as a prominent alternative for combating cancer due to its potent therapeutic effects, minimal side effects, numerous targets, and its crucial role in various stages of cancer treatment. However, challenges such as poor solubility, limited permeability, rapid elimination, instability, low bioavailability, and short half-life hinder its clinical application. To overcome these limitations in the anticancer potential of TCM, recent years have seen the integration of nanotechnology in clinical TCM treatments. Nano-targeted drug delivery systems have assumed an increasingly vital role in cancer therapy by synergizing with the active components of TCM for anticancer treatments. Some TCM-based nano-drug carriers have entered clinical trials or been employed in disease diagnosis and treatment, thereby advancing the field of TCM. In light of this, this article provides an overview of the progress made in applying nano-targeted delivery systems to TCM-based anticancer therapy.
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## 1. Introduction

Cancer now ranks as the second leading cause of mortality, following cardiovascular and cerebrovascular diseases[1]. Currently, there exists a variety of cancer treatment methods, including immunotherapy, radiotherapy, chemotherapy, and surgery. However, each comes with its limitations. For instance, radiotherapy often leads to significant adverse reactions, while surgery remains suitable for only a select group of cancer patients, potentially causing appetite loss and depression among patients[2]. Chemotherapy, the most widely used treatment, is plagued by side effects and the development of drug resistance, adversely affecting both therapeutic effectiveness and patients' quality of life[3]. Hence, the need for alternative and contemporary drug treatments is becoming increasingly urgent.

Traditional Chinese medicine (TCM) has emerged as a prominent alternative therapeutic option owing to its potent efficacy, minimal side effects, and versatility, making it widely applicable in the treatment of cancer patients[4]. Moreover, various components extracted from natural plants within TCM, such as tanshinone (TAN), berberine, artemisinin, resveratrol (RSV), quercetin (QU), tripterygium, and curcumin (CUR), exhibit robust anticancer effects and contribute significantly to various stages of cancer treatment. These components can effectively induce cancer cell apoptosis, inhibit angiogenesis, impede cancer progression, disrupt cancer development, and suppress metastasis[5]. Nevertheless, TCM faces several hurdles, including unpleasant odor, poor solubility, limited permeability, low bioavailability, rapid elimination, instability, short half-life, side effects, and high metabolic rates[6].

In recent years, nano-targeted drug delivery systems have exhibited significant advantages in enhancing the specificity of TCM. These systems improve TCM's bioavailability, facilitate its distribution both *in vivo* and *in vitro*, enhance its pharmacokinetic properties, stabilize it, promote the dissolution of insoluble TCM components, protect it from degradation *in vivo*, increase its therapeutic efficacy, and reduce potential side effects. TCM is now being widely employed across various medical domains[7]. Targeted drug delivery systems consist of three essential components: the drug, drug carrier, and targeting component, all aimed at directing drugs to specific tissues or organs through precise guidance mechanisms. Nano-targeted TCM delivery systems, encompassing liposomes, nanoparticles (NPs), vesicles, mesoporous silica, and micelles, hold great promise in overcoming the current limitations of TCM in anticancer treatments[8]. The amalgamation of different types of nano-targeted drug delivery systems with active TCM ingredients in cancer treatment has elevated the role of TCM's nano-targeted drug delivery system. Moreover, these systems serve as valuable clinical drug carriers. By meticulously regulating drug release and delivering therapeutic agents to solid cancers, they facilitate the study of combining multiple anticancer drugs for codelivery in a single nanocarrier, thus achieving the benefits of combination therapy[9].

In summary, nano-drug targeted systems can be categorized into four main types: passive nano-targeted drug delivery systems, active nano-targeted drug delivery systems, physicochemical nano-targeted drug delivery systems, and bionic nano-drug delivery systems. With the ongoing advancement of nano-drug carriers, several TCM-based nano-drug carriers have entered clinical trials or are being utilized for disease diagnosis and treatment, catalyzing the evolution of TCM[5]. Consequently, this article provides an overview of the application progress of nano-targeted delivery systems in TCM anticancer therapy.

## 2. Passive targeted drug delivery system

In passive targeted drug delivery systems, carriers primarily include lipids, proteins, and biodegradable polymers. These carriers encapsulate drugs within various colloidal systems, forming polymer nanoparticles (PNPs), micelles, liposomes, microemulsions, nanostructured lipid carriers (NLCs), nanovesicles, and other stable structures. The primary aim is to enhance drug concentration within cancer cells, reduce drug dispersion in the bloodstream and other organs, and mitigate toxicity and side effects[10].

The efficacy of passive targeting is particularly pronounced in cancer treatment due to distinct differences between normal and cancerous blood vessels. Normal blood vessels possess a robust structure that prevents large drug particles from escaping into the surrounding tissues. In contrast, cancerous blood vessels often exhibit vascular leakage and disrupted lymphatic circulation, resulting in increased permeability and retention within the tumor vasculature. This phenomenon is conducive to the entry and prolonged presence of nano-targeted delivery systems within cancerous tissues, making passive targeting highly effective against cancer[10].

Following intravenous administration, the distribution of passive targeted drug delivery systems within the body is influenced by particle size. Smaller NPs typically experience limited renal excretion and possess enhanced tissue permeability. For instance, particles of approximately 0.7 μm are frequently intercepted by the pulmonary capillary bed, leading them to accumulate in lung tissue or alveoli. Particles ranging from 0.2 to 3 μm are often taken up by macrophages in the spleen and liver. NPs within the range of 100–200 nm readily accumulate in solid tumors, while those measuring 100 nm can slowly accumulate in bone marrow[11].

### 2.1. Liposomes

Liposomes are vesicles characterized by a hydrophobic double-membrane layer and a hydrophilic inner cavity, making them suitable for encapsulating both fat-soluble and water-soluble drugs. The encapsulation of drugs within liposomes offers several advantages, including the reduction of drug dosage, targeted release, delayed drug release, reduced drug toxicity, alteration of drug distribution within the body, and decreased clearance rate from the body.

Lutein (LUT) is a potential candidate for clinical chemotherapy, but its clinical application is limited due to poor water solubility and rapid excretion. Some studies have developed LUT liposomes coated with vitamin E D-α-tocopherol acid polyethylene glycol 1000 succinate (TPGS). These liposomes promote cell uptake and apoptosis by upregulating the Bax/Bcl-2 ratio, enhancing the cytotoxicity against lung cancer cells while sparing other organs[12]. Consequently, TPGS-coated liposomes represent an effective cancer treatment strategy for poorly water-soluble model drugs like luteolin.

Additionally, a baicalin-coated nano-liposome has been designed for targeted delivery therapy in lung cancer. These nano-liposomes, loaded with baicalin, are prepared

using foam dispersion and lyophilization technology. They exhibit an average particle size of 131.7 ± 11.7 nm, an encapsulation efficiency of 82.8% ± 1.24%, and a yield of 90.47% ± 0.93%. These nano-liposomes provide stable, sustained release for 24 h and display no hemolytic activity *in vitro*. After intravenous injection, baicalin nano-liposomes show the highest concentration in the lungs at different time points, with lung targeting efficacy being 14.131, 3.470, 1.893, and 3.357 times higher than that in plasma, kidney, liver, and spleen, respectively. Furthermore, baicalin nano-liposomes exhibit no toxic effects on normal lung tissue. In an anticancer treatment study using human lung cancer nude mice, baicalin-containing nano-liposomes demonstrate superior efficacy, significantly extending median survival time (25.90 ± 0.53 d) compared to blank liposomes (11.40 ± 0.16 d) and baicalin solution (17.30 ± 0.47 d). Consequently, baicalin-carrying nano-liposomes hold promise as an effective drug carrier with excellent lung targeting capabilities and therapeutic potential against lung cancer and other lung diseases[13].

In a study by Fu et al.[14], targeted liposomes containing daunorubicin and emodin are prepared by modifying arginine-glycine-aspartic acid (RGD) to evaluate their efficacy against highly aggressive breast cancer. The results reveal that RGD-modified daunorubicin and emodin liposomes exhibit a high encapsulation rate, small volume, and uniform distribution. The combination of these two targeted liposomes demonstrates potent toxicity against highly aggressive breast cancer cells and selectively accumulates at the cancer site. This selective accumulation effectively inhibits the formation of cancer blood vessels and the metastasis of cancer cells, thus exerting an anticancer effect. Further investigations into the mechanism of action reveal that daunorubicin and emodin liposomes down-regulate certain migration-related proteins, including matrix metalloproteinase-2 (MMP-2), vascular endothelial cadherin (VE-Cad), transforming growth factor-β1 (TGF-β1), and hypoxia-inducible factor-1α (HIF-1α). Targeted liposomes enable the precise delivery of chemotherapy drugs. Consequently, the combination of daunorubicin and emodin liposomes holds promise as a potential treatment for aggressive breast cancer.

The development of drug resistance is a significant factor contributing to treatment failures in cancer. Meng et al.[15] co-encapsulated RSV and paclitaxel (PTX) in pegylated liposomes for combined treatment of drug-resistant cancer. This approach exhibits robust cytotoxicity against drug-resistant MCF-7/ADR cancer cells *in vitro*, enhancing drug bioavailability and improving therapeutic efficacy against drug-resistant cancer.

### 2.2. PNPs

In a study conducted by Bao et al.[16], researchers have investigated an RGD-modified nano-drug delivery system combining hesperidin and atorvastatin (RGD-ATST/TAGE-CNPs) for the concurrent treatment of colon cancer. The system employs polyethylene glycol as a linking agent to facilitate the integration of RGD-modified hesperidin and atorvastatin into the nano-drug delivery system RGD-ATST/TAGE-CNPs, which is then utilized to treat colon cancer cells and colon cancer mouse models. The results indicate that this nano-system exhibits a high encapsulation rate, approximately 90%, and possesses a robust drug-loading capacity. Moreover, it demonstrates a stronger cytotoxic effect on colon cancer cells compared to unmodified drugs while showing no significant difference in toxicity toward normal cells. The greatest synergistic effect is observed when the weight ratio of hesperidin to atorvastatin is maintained at 1:1.

Additionally, RGD-ATST/TAGE CNPs exhibit high biological distribution at the cancer site *in vivo* and

significantly inhibit cancer growth. Importantly, this nano-drug delivery system displays a significant synergistic therapeutic effect without causing apparent toxicity to major organs and tissues, suggesting its potential application in colon cancer treatment.

### 2.3. Lipid-polymer hybrid nanoparticles (LPNs)

Polymers used in LPNs encompass natural biopolymers, semi-synthetic polymers, and synthetic polymers. Lipids offer favorable properties for drug delivery systems, particularly in oral applications. They enhance bioavailability by prolonging gastrointestinal residence time, stimulating biliary and pancreatic secretions, reducing metabolism, improving intestinal permeability, and facilitating lymphatic transport[17]. Consequently, the fusion of polymer structures with the biological attributes of lipids results in drug carriers of significant therapeutic value.

In the context of non-Hodgkin lymphoma, chemotherapy remains the standard treatment. Zhu et al.[18] have developed LPNs capable of co-delivering vincristine (VCR) and QU (VCR/QU LPNs) for combination chemotherapy in lymphoma. Experimental results showcase that VCR/QU LPNs exhibit negative zeta potential, nanoscale dimensions, and *in vitro* sustained release characteristics. *In vivo* and *in vitro* assessments reveal a more potent anti-lymphoma effect for VCR/QU LPNs, signifying their ability to synergistically harness the therapeutic potential of two distinct drugs. This approach involving QU and VCR within the same LPNs presents a promising strategy to overcome chemotherapy resistance in lymphoma.

Another study by Li et al.[19] features the preparation of two nanocarriers simultaneously delivering CUR and cisplatin: PNPs and LPNs. Comparisons of the anticancer effects of PNPs and LPNs on human cervical adenocarcinoma cells (HeLa cells) and mouse cervical cancer models reveal that LPNs exert the most potent toxicity against cancer cells *in vitro* and display superior anticancer effects *in vivo*. Consequently, LPNs hold promise as codelivery systems for synergistically targeting cancer nanomedicines.

Ruttala et al.[20] have adopted a different approach to prepare LPNs co-containing CUR and PTX. They encapsulate albumin NPs loaded with PTX within a polyethylene glycol hybrid liposome containing CUR using thin film hydration technology. This ensures the sequential and continuous release of CUR and PTX. CUR enhances the efficacy of PTX by down-regulating the nuclear factor NF-κB and Akt pathways. The PEGylated hybrid liposome containing CUR induces cancer cell apoptosis and cell cycle arrest in the G2/M phase. Combining PTX, a potent anticancer drug, and CUR, an NF-κB inhibitor, within an LPN system significantly heightens anticancer efficacy.

### 2.4. NLCs

NLCs are lipid nanoparticles composed of liquid lipids, solid lipids, and surfactants, known for their excellent drug-loading capacity and sustained release properties. Kebebe et al.[21] have developed NLCs loaded with Gambogic acid (GA) (GA-NLCs) with a particle size of approximately 20 nm. The results indicate that GA-NLCs exhibit enhanced anticancer activity and improved targeting against breast cancer.

Zhang et al.[22] have formulated NLCs loaded with doxorubicin (DOX) and salvianolic acid A (Sal A) (E-[c(RGDfK)]/FA-NLC-Sal A/DOX). They compare the effects of this treatment on various cancer cells, including different breast cancer cells and non-small cell lung cancer cells. The findings demonstrate that, compared to the normal saline group, the treatment induces a high rate of cancer cell apoptosis (61.30%), significant inhibition of cancer weight (83.94%), a remarkable reduction in

cancer volume (90.72%), and lower kidney toxicity. Furthermore, Sal A mitigates the nephrotoxic effects of DOX, reducing serum creatinine concentration by 61.64% in the free DOX group. In the NLC group, Sal A reduces creatinine levels by 42.47% compared to the DOX group. Additionally, the modification of E-[c(RGDfK)]/FA significantly reduces the kidney-related side effects of the drugs. In the E-[c(RGDfK)]/FA-NLC-Sal A/DOX group, serum creatinine concentration is 46.35% lower than that in the NLC-Sal A/DOX group. These results suggest that E-[c(RGDfK)]/FA-NLC-Sal A/DOX not only enhances anticancer efficacy but also improves tolerance to chemotherapy. In another study, NLCs modified with hyaluronic acid (HA) are engineered as nanocarriers co-delivering baicalein (BCL) and DOX (HA-BCL/DOX-NLCs). The findings indicate that HA-BCL/DOX-NLCs also exhibit a potent synergistic effect and strong anticancer activity against breast cancer cells[23].

Jiang et al.[24] have prepared NLCs loaded with CUR and etoposide (ETP) using solvent injection technology, achieving drug loadings of 82% for CUR and 83% for EPT. Compared to other formulations, including ETP NLCs, ETP solution, and NLCs, ETP-CUR NLCs demonstrate the highest cytotoxicity in gastric cancer cells *in vitro* and accumulate efficiently in gastric cancer tissues *in vivo*. Moreover, the low cytotoxicity of ETP-CUR NLCs in normal tissues suggests their potential as an effective treatment for gastric cancer.

### 2.5. Mesoporous silica nanoparticles (MSNs)

MSNs are widely employed as drug carriers due to their uniform and adjustable pore size, large specific surface area, stable structure, high drug loading capacity, and biocompatibility. Ent-11α-hydroxy-15-oxo-kaur-16-en-19-oic-acid (5F) is a diterpenoid compound extracted from hemipleuron, known for its anticancer effects against various malignant cancer cells and its ability to induce cancer cell apoptosis. However, 5F is a small anticancer drug, and there have been limited reports on its *in vivo* anticancer efficacy. Liu et al.[25] have loaded 5F onto fluorescent MSNs for the targeting and treatment of nasopharyngeal carcinoma in nude mice. The results demonstrate effective uptake of 5F by transplanted nasopharyngeal carcinoma, leading to a significant inhibition of cancer growth.

To enhance the bioavailability and anti-leukemia efficacy of tanshinone IIA (TanIIA) following oral administration, Li et al.[26] have employed biotinylated lipid bilayer-coated MSNs as carriers (TanIIA@Bio-LB-MSNs). *In vitro* release studies reveal a significantly higher release of TanIIA from TanIIA@Bio-LB-MSNs compared to free TanIIA. Cell uptake studies with Caco-2 cells show increased TanIIA uptake, leading to enhanced anti-leukemia activity *in vitro*. Further modification with biotin on TanIIA@MSNs (TanIIA@Bio-LB-MSNs) improves apparent in-situ permeability by 1.6 times. After oral administration of TanIIA@Bio-LB-MSNs, the area under the blood concentration-time curve for TanIIA is 3.4 and 1.9 times larger than that of pure TanIIA and TanIIA@MSNs groups, respectively. These findings indicate that MSNs significantly enhance the bioavailability and anti-leukemia activity of oral TanIIA, and biotin modification further improves its bioavailability and anticancer efficacy.

### 2.6. Micellar systems

Nanomicelles are NPs characterized by a unique core-shell structure formed through the self-assembly of amphiphilic molecules under specific conditions. This micellar system addresses the challenge of enhancing the solubility of drugs with low water solubility while extending their circulation time *in vivo* by encapsulating hydrophobic drugs within micellar cores.

Cantharidin (CTD), the primary active compound in Mylabris, a toxic Chinese medicine, exhibits significant therapeutic potential against hepatocellular carcinoma. However, the toxic effects of CTD on the urinary and digestive systems have limited its clinical application. To mitigate these issues, Yao et al.[27] have developed CTD-loaded micelles (mPEG-PLGA-CTD) to reduce CTD toxicity and enhance its anticancer efficacy. mPEG-PLGA-CTD consists of uniform spherical particles with a diameter of 25.32 ± 1.25 nm, exhibiting excellent biocompatibility and stability. The formulation extends drug circulation half-life, increases drug accumulation in cancer tissues, and significantly reduces drug accumulation in other organs, such as the kidneys. mPEG-PLGA-CTD inhibits liver cancer cells by suppressing protein phosphatases 2A and promoting cell apoptosis. In the realm of liver cancer targeted therapy, Chen et al.[28] have devised a dual-responsive micelle system capable of achieving liver cancer targeting and intracellular drug release in response to redox stimuli. The results demonstrate that TanIIA can accumulate and release more rapidly within liver cancer cells. Furthermore, through the up-regulation of caspase 3/7 and P38 proteins, elevation of intracellular reactive oxygen species (ROS) levels, and promotion of cell necrosis, this approach effectively inhibits cancer growth and prolongs the survival time of mice.

### 2.7. Microemulsion

Microemulsion, also known as nanoemulsion, is a thermostable, low-viscosity, isotropic dispersion system composed of a water phase, co-emulsifier, oil phase, and emulsifier. It is translucent or transparent and serves as an ideal drug carrier, offering advantages such as good dispersion, absorption, and high bioavailability.

Zhang et al.[29] have developed an intravenously loaded microemulsion containing β-elemene and celastrol. The results indicate that β-elemene can be employed as an oil phase to improve the drug loading rate while optimizing the mass ratio of β-elemene to triptolithol. In both *in vitro* and *in vivo* experiments, the dual drug-loaded microemulsion exhibits a synergistic anti-proliferation effect on lung cancer cells, resulting in a higher apoptosis rate.

Qu et al.[30] have utilized coix polysaccharide (CP) and coix seed oil as functional excipients and anticancer components to create a microemulsion drug delivery system targeting liver cancer. This system enhances cancer-specific accumulation through CP-mediated passive cancer-targeting enhancement. The semi-maximum inhibitory concentration of liver cancer cells is found to be 70.2 μg/mL, significantly inducing cancer cell apoptosis, inhibiting cancer growth, and prolonging survival time.

Wang et al.[31] have developed a bi-functional microemulsion (AS1411/SKN&DTX-M) containing shikonin and docetaxel, capable of penetrating the blood-brain barrier. AS1411/SKN&DTX-M can target gliomas with CD44/nucleoprotein overexpression, induce apoptosis in glioma cells, and inhibit their growth. In an artificial blood-brain barrier model, AS1411/SKN&DTX-M reduces transdermal resistance and improves the apparent permeability coefficient, offering an effective treatment approach for intracranial glioma with these drugs.

## 3. Active targeted drug delivery system

Active targeting agents utilize monoclonal antibodies or ligands to modify the surface of NPs, enabling the selective delivery of drugs to specific target areas. This allows drugs to accumulate actively in cancer cells and exert their therapeutic effects. The active targeting of NPs is advantageous due to variations in

receptor expression and other biological characteristics between normal cells and cancer cells. For instance, cancer tissues or cell surfaces often exhibit an overexpression of transferrin receptors and folate receptors. Consequently, active targeted drug delivery systems ensure that the drug exclusively acts on cancer cells while also facilitating the passage of NPs through physiological barriers such as the blood-brain barrier or intestinal mucosa[32].

### 3.1. Transferrin (Tf)-modified nanocarriers

Tf receptors are typically present in both cancer and normal cells, but cancer cells tend to exhibit approximately five times higher expression levels of Tf receptors on their surfaces compared to normal cells. Tf can bind to these Tf receptors, facilitating its internalization into the cell and allowing it to reach its intended target site.

A study by Guo et al.[33] has developed Coix seed oil and Tripterine coloaded microemulsions with a Tf modification (Tf-CT-MEs), which have demonstrated improved efficacy in treating cervical cancer. In serum, Tf-CT-MEs exhibit a significant synergistic anticancer effect and display excellent stability, ultimately leading to a notable slowdown in cancer growth. Further investigations reveal that Tf-CT-MEs induce apoptosis, enhance anti-angiogenesis, and inhibit cancer cell proliferation by activating the caspase-3 pathway and regulating the balance between bax and bcl-2. Additionally, the concentrations of CCL2, TGF-β1, IL-6, and TNF-α in serum are reduced by 26.9%, 27.7%, 42.5%, and 61.2%, respectively, suggesting significant potential as an effective treatment for cervical cancer.

In another study by Cui et al.[34], Tf-modified NPs (Tf-PEG CUR-DOX NPs) are designed for co-delivering CUR and DOX to treat breast cancer. The results indicate that Tf-PEG-CUR/DOX NPs have a more pronounced cytotoxic effect on breast cancer cells compared to Tf-PEG-CUR NPs alone. Moreover, Tf-PEG CUR-DOX NPs exhibit higher accumulation in breast cancer tissues compared to injected CUR-DOX, resulting in greater anticancer efficacy both *in vitro* and *in vivo*. This approach not only achieves more efficient cancer-targeted drug delivery but also reduces cytotoxicity.

### 3.2. Folic acid (FA)-modified nanocarriers

Similar to the distribution of Tf receptors on the surface of cancer cell membranes, folate receptors are overexpressed in cancer cells, with significantly higher activity than in normal cells. Moreover, FA possesses attributes such as low immunogenicity, high modifiability, and excellent storage stability. Exploiting these disparities in folate receptor expression between cancer sites and normal tissues enables the targeted delivery of folate-modified drugs to cancer cells.

Bufallin (BUF) is an effective TCM component known for its anticancer properties, particularly in breast cancer. However, its high toxicity and poor solubility have restricted its application. Some studies have designed FA-modified nanocarriers (FA-MOF/BUF) for the encapsulation of BUF. The results indicate that compared to free BUF, FA-MOF/BUF NPs offer enhanced stability, water solubility, increased intracellular uptake, and greater cytotoxicity in breast cancer cells. This, in turn, bolsters their anti-breast cancer activity while mitigating side effects[35].

Nitidine chloride (NC) is another TCM ingredient with anticancer potential but can yield unacceptable side effects at therapeutic doses. Li et al.[36] have developed folate-modified D-α-tocopheryl polyethylene glycol 1000 succinate (TPGS-FA) as a nanocarrier for drug delivery (TPGS-FA/NC). Results demonstrate that TPGS-FA/NC NPs release NC in a controlled and

sustained manner, significantly enhancing its toxic effect on hepatocellular carcinoma cells compared to free nitidine chloride. This suggests that TPGS-FA/NC may serve as an effective and safe treatment for hepatocellular carcinoma.

Arsenic trioxide (ATO) is an active ingredient in TCM known for its efficacy against hepatocellular carcinoma. However, due to its high toxicity and poor distribution, clinical application has been limited. Consequently, studies have been undertaken to prepare FA-modified liposome-coated calcium arsenate NPs (FA-LP-CaAs). The results reveal that the cancer microenvironment, characterized by folate receptors on cell membranes and overexpression of MMP2 in the extracellular matrix, promotes drug uptake and accumulation in cancer cells. Additionally, in the mildly acidic cancer environment, the degraded products of FA-LP-CaAs can escape from lysosomes, resulting in a more potent anticancer effect with reduced toxicity[37].

The findings from Lan et al.[38] regarding folate-modified NPs containing ursolic acid (UA) and Methotrexate (MTX) indicate significant improvements in water solubility when compared to free UA or MTX. Moreover, UA-MTX-NPs exhibit a faster drug release rate in acidic environments (pH 5.0) compared to neutral pH (pH 7.4), suggesting their ability to rapidly release drugs in the acidic conditions of the cancer microenvironment. UA-MTX NPs exhibit a high level of folate receptor targeting in breast cancer cells. Apoptosis and cytotoxicity experiments reveal that UA-MTX NPs display enhanced antiproliferative effects on breast cancer cells overexpressing folate receptors when compared to free drugs. Furthermore, combined therapy demonstrates improved anticancer efficacy.

Li et al.[39] have modified the surface of MSNs using polyethyleneimine-FA (PEI-FA) or HA through disulfide bonds. This leads to the development of a novel nanocarrier system for targeting cancer and controlling the release of CUR-MSN/CUR-PEI-FA and MSN/CUR-HA, respectively. These nanocarriers exhibit cytotoxicity to breast cancer cells and enhanced cancer cell uptake when compared to non-targeted nanocarriers. Real-time imaging demonstrates that MSN-PEI-FA has higher accumulation and more precise targeting than MSN-HA, with MSN/CUR-PEI-FA displaying a higher degree of cancer growth inhibition compared to free CUR. Therefore, MSN/CUR-PEI-FA stands out as a promising nano-drug delivery system for breast cancer treatment.

In a study by Li et al.[40], FA-modified PEGylated liposome-bilayer (LB) membrane-coated MSNs are prepared. This FA-LB-MSNs active targeted drug delivery system achieves a drug loading of 5.5% for PTX and 1.8% for TAN IIA. The results indicate synchronized release of PTX and TAN IIA from the carrier, resulting in a strong synergistic effect between the two drugs that promote apoptosis and differentiation of leukemia cells. This study further confirms the synergistic therapeutic effect of PTX and TAN IIA on human acute promyelocytic leukemia and highlights the advantages of FA-LB-MSNs as coloaded nanocarriers in cancer-targeted therapy.

### 3.3. Cell-penetrating modified nanocarriers

Cell-penetrating peptides (CPPs) have emerged as highly promising ligands in cancer-targeted therapy, showing great potential as carriers for cancer drugs. In some studies, CPP RGERPPR has been used to modify luteo-supported nanocarriers (GA-NLC). This modification results in enhanced uptake and toxicity in breast cancer cells. GA-NLC exhibits a more significant inhibition of cancer growth compared to the control group, indicating that RGERPPR has the potential to serve as a carrier for targeted drug delivery in anticancer therapy[41].

Research has also focused on Artesunate NPs (HA-R6H4-NLC/ART) modified with both HA and the CPP R6H4-SA. The results demonstrate that R6H4-SA significantly improves the uptake of nanocarriers by liver cancer cells, enhancing their anticancer effects and exhibiting targeting capabilities. This suggests that HA-R6H4-NLC/ART may serve as an efficient, targeted anticancer drug delivery system, effectively recognizing and penetrating cancer cell membranes[42].

Chen et al.[43] have developed a nano-delivery system using the iRGD CPP to modify encapsulated JQ1 (a BET inhibitor) and oridonin (ORI, an active diterpenoid from Chinese medicine) (iRGD-PSS@PBAE@JQ1/ORI NPs). The results show that iRGD-PSS@PBAE@JQ1/ORI NPs effectively enhance cell internalization and cancer targeting of JQ1 and ORI. ORI exhibits various anticancer effects, including inhibiting intracellular ROS generation, anticancer cell proliferation, and inhibiting lactic acid secretion. On the other hand, JQ1 can reverse immune tolerance by inhibiting the expression of PD-L1. The modification with the CPP significantly improves the cancer penetration and cell internalization of the nanodelivery system, and the combination of ORI and JQ1 has a synergistic anticancer effect, thereby enhancing anti-breast cancer efficacy.

In contrast, Wang et al.[44] have developed a targeted delivery system for daunorubicin and dioscin, modified with the PFV cell transmembrane peptide using a membrane dispersion and ammonium sulfate gradient method. The results indicate excellent physical and chemical properties, significantly enhancing the uptake capacity of target cells and increasing cytotoxicity to cancer cells. Dioscin encapsulation further promotes daunorubicin's enhancement of non-small cell lung cancer cells and angiogenesis inhibition. It also inhibits cancer metastasis by down-regulating TGF-β1, MMP-2, HIF-1α, and VE-cadherin. This codelivery system of daunorubicin and dioscin demonstrates a clear anticancer effect in cancer-bearing mice. Targeting daunorubicin and dioscin codelivery systems may prove to be an effective strategy for treating non-small cell lung cancer.

## 4. Physicochemical nano-targeted drug delivery system

Physicochemical targeting involves the incorporation of various materials onto the surface of nanoparticles, such as magnetic, pH-sensitive, temperature-sensitive, ultrasonic-responsive, and electromagnetic wave-responsive materials. This modification enables NPs to respond to a range of stimuli both inside and outside the body, including changes in pH, exposure to electromagnetic radiation, fluctuations in temperature, exposure to ultrasonic waves, external magnetic fields, and infrared radiation. These responses enhance drug concentration at the target site and enable the drug to act directly on the desired area. Simultaneously, the use of physicochemical targeting strategies can help reduce the occurrence of adverse reactions[45]. Currently, magnetic nanoparticles, light-sensitive nanoparticles, and pH-sensitive NPs are among the most commonly studied in this context.

### 4.1. pH-sensitive NPs

Given that orally administered drugs must traverse the highly acidic environment of the stomach (pH 1.3–2.5) before entering the neutral to weakly alkaline environment of the intestine (pH 5.1–7.8), it is feasible to design pH-sensitive NPs containing Chinese medicine to respond to these pH variations. This design can facilitate the development of an effective nano-drug delivery system.

Intravenously administered drugs enter the neutral to weakly alkaline blood or tissue environment (pH 7.23),

whereas cancer tissues typically exist in a slightly acidic environment (pH 6.0–7.0). Therefore, pH-sensitive NPs can be specifically targeted to cancer sites, capitalizing on the unique conditions of the cancer microenvironment before releasing their payload.

For instance, Zhang et al.[46] have developed pH-sensitive NPs for a codelivery system containing DOX and CUR. In both human umbilical vein endothelial cells and human liver cancer cells, Dox-Cur NPs exhibit significantly enhanced release and improved cell internalization within the acidic environment of cancer cells compared to free drugs. Consequently, pH-sensitive NPs can effectively synergistically inhibit cancer.

Similarly, Yang et al.[47] have conducted a study on pH-sensitive NPs to enhance the anticancer effects of CUR. Their system can intelligently modify the surface charge and size of CUR. The nano-drug delivery system comprises methoxy poly(ethylene glycol)-poly(lactide)-poly(β-amino ester) (MPEG-PLA-PAE) copolymers. When exposed to an acidic medium (with a decrease in pH from 7.4 to 5.5), the surface charge increases to 24.8 mV, and the particle size decreases from 171.0 to 22.6 nm. This alteration promotes better cancer penetration and increases the uptake of CUR by human breast cancer cells. Furthermore, their results demonstrate that MPEG-PLA-PAE extends *in vivo* circulation time, resulting in more specific accumulation in cancer tissues and leading to more substantial suppression of cancer growth.

In another study, Duan et al.[48] have developed three cancer-targeting NPs loaded with ORI, each with different galactose levels. *In vitro* tests reveal that ORI release from the NPs correlates with pH, releasing more under weakly acidic conditions. The cytotoxicity of the NPs is also pH-sensitive. The pH-sensitive NPs loaded with ORI exhibit more robust anticancer activity in hepatocellular carcinoma cells, with activity increasing alongside the number of galactose molecules. These findings suggest that galactose-modified pH-sensitive NPs are suitable for targeted drug delivery to hepatocellular carcinoma cells.

Lastly, Sun et al.[49] have produced pH-sensitive NPs loaded with DOX and TAN using emulsification and solvent diffusion. Their results demonstrated that these NPs released DOX and TAN more rapidly, leading to a stronger inhibitory effect on cancer growth. These NPs are absorbed by prostate cancer cells at a rate as high as 58.9% ± 1.9%, exhibit high distribution within cancer tissue, and result in a more potent anticancer effect, offering a promising approach for dual drug delivery to prostate cancer cells.

### 4.2. Magnetic NPs

Magnetic NPs involve the incorporation of magnetic materials into NPs, enabling them to be guided to specific target areas within the body using an external magnetic field. This technique facilitates controlled and targeted drug release, as the drugs are released gradually without the need for a magnetic field. Consequently, magnetic NPs exhibit strong targeting and controlled release properties. $Fe_3O_4$ magnetic NPs are extensively employed in biomedical applications due to their biocompatibility, high magnetic saturation, and ease of size manipulation. Researchers have also explored the creation of composite NPs, such as ferro tetroxide/bismuth sulfide NPs ($Fe_3O_4$@PDA)-HCPT, which enhances their photothermal effects and demonstrates significant anticancer efficacy against esophageal cancer cells and mice with esophageal cancer[50].

Both sulforaphane and CUR possess anticancer properties, yet their application is restricted by poor oral bioavailability and limited water solubility. To enhance the solubility and bioavailability of sulforaphane and CUR, Danafar et al.[51] have employed a combined

administration approach, incorporating these compounds into $Fe_3O_4$ magnetic NPs, specifically PEGylated $Fe_3O_4$@Au NPs. The results reveal that PEGylated $Fe_3O_4$@Au NPs have an average particle size of 80.57 nm and a zeta potential of approximately –15.4 mV. These NPs exhibit monodispersity in water, showcasing high stability and efficient drug loading. The drug loading and encapsulation efficiency for sulforaphane and CUR are found to be 16.74% ± 0.02%, 17.32% ± 0.02%, and 81.20% ± 0.18%, 83.72% ± 0.14%, respectively. *In vitro* experiments conducted on human breast adenocarcinoma cells (MCF-7) demonstrate that PEGylated $Fe_3O_4$@Au NPs significantly enhance the anticancer effects of sulforaphane and CUR, inducing cancer cell necrosis, apoptosis, and inhibiting migration.

Delivery of therapeutics to treat gliomas is challenging due to the presence of the blood-brain barrier. A nanoparticle containing $Fe_3O_4$, docetaxel, and shikonin ($Fe_3O_4$@T7/AS1411/DTX&SKN-M) is designed for glioma treatment. Results show that these NPs can accumulate in the brain with the aid of an external magnetic field, effectively inhibiting glioma growth and extending survival. Consequently, magnetic modification for targeted delivery of docetaxel and shikonin to gliomas presents a promising approach for precise and synergistic glioma treatment[52].

### 4.3. Light-sensitive NPs

Light-sensitive NPs achieve their light-responsive behavior by incorporating light-sensitive chemical groups into their structure and utilizing high-intensity ultraviolet light with a wavelength of ≤ 360 nm. Researchers have developed a photosensitive treatment for colon cancer using a combination of Astragaloside III (As) and the photosensitizer chlorine e6 (Ce6), creating ((As + Ce6)@MSNs-PEG) NPs. The results demonstrate that (As + Ce6)@MSNs-PEG can effectively penetrate cancer cells, induce immune cell infiltration, enhance the cytotoxicity of $CD^{8+}$ T cells and natural killer cells *in vivo*, as well as activate NK cells to inhibit the proliferation of colon cancer cells. This treatment also extends the lifespan of cancer-bearing mice without causing significant side effects. Therefore, (As + Ce6)@MSNs-PEG stands as a safe and effective NP for colon cancer treatment[53].

An innovative and promising approach to anticancer therapy involves the development of carrier-free nanomedicine through the supramolecular self-assembly of pure drugs. In this context, the photosensitizer Ce6 and the small hydrophobic anticancer drug 10-hydroxycamptothecin (HCPT) have been directly assembled into discrete and stable nanoparticles. This approach not only combines two different anticancer strategies into a single delivery system but also mitigates the extreme hydrophobicity associated with HCPT. Wen et al.[54] have further explored different ratios of Ce6 and HCPT to determine the optimal nano-formulation. The prepared HCPT/Ce6 NPs exhibit a surface charge of approximately –33 mV, with uniform size (approximately 360 nm in length and 135 nm in width). Results indicate that the antiproliferative effect of HCPT/Ce6 NPs on breast cancer cells (4T1, MCF-7 cells) and lung cancer cells (A549 cells) without laser irradiation is comparable to that of free HCPT. However, in the presence of laser irradiation, HCPT/Ce6 NPs significantly inhibit cancer cell proliferation. *In vivo* experiments also demonstrate significant anticancer effects, with HCPT/Ce6 NPs nearly completely suppressing cancer growth in mice. Hence, this carrier-free photosensitive nanomedicine, prepared through a self-assembly method, holds promise for advancing chemical-photodynamic combination therapy in cancer treatment.

## 5. Bionic nano-drug delivery system

The bionic nano-drug delivery system relies on natural particle carriers, which possess attributes like low immunogenicity and high targeting specificity. This innovative system can mimic the functions and structures of viruses, cells, and other biological components in the body, replicating their processes to effectively deliver encapsulated drugs to specific cancerous regions and exert anticancer effects. Current research in this field primarily concentrates on utilizing endogenous proteins, mammalian cells, exosomes, and other biological entities for drug delivery.

### 5.1. Mammalian cell-based nano-drug delivery system

The use of a nanometer drug delivery system based on mammalian cells leverages carriers such as red blood cells, stem cells, macrophages, and platelets. These carriers possess distinct attributes, including low immunogenicity, excellent biocompatibility, degradability, strong targeting capabilities, and high drug-loading capacity.

For instance, red blood cells have a unique double-sided concave disk structure, and their membranes can envelop nanocarriers, allowing them to mimic endogenous substances. This disguise helps avoid recognition by phagocytes of the reticuloendothelial system *in vivo*, extending the circulation time of these carriers in the bloodstream. Studies have shown that nanocarriers containing angelica polysaccharides and CUR encapsulated within erythrocyte membranes exhibit excellent biocompatibility and drug-loading capabilities. In both *in vivo* and *in vitro* experiments, these carriers promote the expression of immune factors like IL-12, TNF-α, and IFN-γ, enhance the infiltration of $CD^{8+}$ T cells, and demonstrate strong targeting abilities for effective anti-liver cancer treatment[55].

RSV is known for its anticancer properties by targeting cancer cell metabolism and promoting mitochondrial electron transport chain overload, leading to increased ROS production. In colorectal cancer cells, RSV has been shown to upregulate active oxygen and lipid peroxidation, down-regulate the expression of glutathione peroxidase 4 (GPX4) and solute carrier family 7 member 11 (SLC7A11) proteins, and ultimately inhibit cancer cell growth. To improve the delivery efficiency of RSV, Ma et al.[56] have developed a bionic nanocore by coating RSV-supported poly(ε-caprolactone)-polyethylene glycol (PCL-PEG) NPs with erythrocyte membranes (RSV-NPs@RBCm). This approach enhances biocompatibility, evades immune cell detection, and improves water solubility, offering a promising drug delivery method for colorectal cancer treatment.

Moreover, Zhang et al.[57] have created a bionic nanocore with glycyrrhizin by combining erythrocyte membranes and synthetic polymer nuclei. This formulation improves biocompatibility, stability, and circulation time, enhancing the anti-colon cancer efficacy of glycyrrhizin.

Platelet membrane (PLTM) expresses CD47 protein, which prevents phagocytosis by macrophages. Biomimetic PLTM-based nano-drug delivery systems aim to promote drug retention and avoid macrophage uptake while minimizing immunogenicity. PLTM also overexpresses *P*-selectin, facilitating the binding of these systems to CD44 receptors overexpressed by cancer cells. For example, NPs (PLTM-CS-PPLGA/Bu NPs) loaded with the anti-cancer drug BUF and coated with PLTMs have been developed. These NPs exhibit a similar protein composition as PLTM, with a particle size of about 192 nm. They demonstrate significantly higher uptake in hepatocellular carcinoma cells compared to uncoated NPs due to the active targeting effect, resulting in enhanced anticancer effects. This approach holds promise for targeted cancer therapy[58].

Hederagenin (HED) exhibits relatively weak anticancer activity, with its specific mechanism still unclear. To address this limitation, Shang et al.[59] have prepared NPs carrying ivy saponin coated with PLTM (PLT@BPQDs-HED). The PLTM acts as a shell to target cancer sites and significantly enhance anticancer activity. These NPs can promote the production of intracellular ROS, inhibit cancer cell viability and mitochondrial membrane potential, reduce the number of proliferative Ki-67 positive cells, induce cytochrome C release, down-regulate anti-apoptotic Bcl-2, and upregulate pro-apoptotic Bax. Additionally, they activate caspase-3 and caspase-9, promote autophagosome formation, induce the transformation of autophagy protein LC3-I to LC3-II, and upregulate Beclin-1. Overall, PLT@BPQDs-HED significantly enhances cancer targeting and promotes mitochondria-mediated autophagy and apoptosis in cancer cells.

### 5.2. Nano-drug delivery system based on endogenous protein

Proteins constitute a vital component of the human biological structure. Endogenous proteins, each with distinct functions, can be harnessed for drug delivery systems. Notably, lipoproteins and albumin serve as key players in these systems.

Endogenous lipoproteins have garnered significant attention as efficient transport carriers. Modern synthetic nanocarriers closely emulate the structure of lipoproteins, allowing for targeted drug delivery through techniques like core embedding and surface modification. Low-density lipoprotein (LDL) receptors are ubiquitous in various cell and tissue types, with cancer cells often overexpressing them. LDL, an endogenous NPs, offers excellent biocompatibility, biodegradability, and low immunogenicity, thus avoiding recognition and clearance by the endogenous reticuloendothelial system *in vivo*.

For instance, Zhang et al.[60] have developed LDL-mediated NPs (Ost/LDL-NSC-NPS) loaded with osthole (Ost). These NPs exhibit a high encapsulation efficiency of 78.28% ± 2.06%, with an average particle size of approximately 145 nm and a drug loading of 18.09% ± 0.17%. *In vitro* release studies demonstrate prolonged drug release compared to natural materials. In liver cancer cells, Ost/LDL-NSC-NPs show a 24-h maximum median inhibitory concentration that is only 16.23% of that observed with free Ost. Fructus cnidii can inhibit the proliferation of hepatocellular carcinoma cells by promoting apoptosis and inhibiting cancer cells during the synthetic phase of the cell cycle. Cellular uptake studies, subcellular localization, and *in vivo* near-infrared fluorescence imaging all confirm the strong targeting capability of Ost/LDL-NSC-NPs. Therefore, LDL-NSC-NPs emerge as a promising targeted drug delivery system for liver cancer.

Serum albumin boasts a network-like porous structure capable of effectively encapsulating drugs. Moreover, albumin is non-immunogenic, safe, non-toxic, and exhibits excellent biocompatibility and biodegradability. Li et al.[61] have developed a liver-targeting albumin nanoparticle drug delivery system (ORI-GB-NPs) by inserting NPs containing ORI into the interstitial spaces of albumin and covalently binding galactose to albumin. The resulting NPs have a negative charge, a zeta potential of approximately –30 mV, and a particle size below 200 nm. ORI-GB-NPs prove efficient in transporting poorly soluble anticancer drugs to cancer sites. These drugs are dispersed in the NPs in an amorphous form, ensuring slow degradation and release upon reaching the cancer site in the presence of albumin. This indicates that ORI-GB-NPs possess favorable physical and chemical properties and serve as a stable targeted delivery system for the insoluble anticancer drug raborunitrin.

### 5.3. Exosome-related nano-drug delivery system

In recent years, exosomes have emerged as promising nanocarriers for delivering drugs to treat cancer. Exosomes are characterized by their small size and phospholipid bilayer structure. They originate from the secretion of the body's own cells, which makes them resistant to enzymatic degradation and prolongs the half-life of drugs during the delivery process. Exosomes also have a natural affinity for target cells, ensuring effective drug delivery to cancer cells.

Triptolide (TP) possesses anticancer properties, but its clinical application is limited due to hepatorenal toxicity and poor water solubility. To address this, a TP-loaded exosome delivery system (TP-Exos) has been developed to investigate its impact on the proliferation and apoptosis of ovarian cancer cells. The efficacy of TP-Exos in treating ovarian cancer is assessed through *in vivo* cancer targeting studies involving exosomes, monitoring cancer size in mice, and conducting TUNEL apoptosis tests. Additionally, the toxicity of TP-Exos is evaluated through histopathological analysis of the liver, renal function tests, and examination of major organs such as the kidney, liver, heart, spleen, lung, and ovary. The results demonstrate that TP-Exos retains the characteristics of exosomes and exhibits high drug encapsulation efficiency. They are taken up by ovarian cancer cells and effectively accumulated at the cancer site. While the apoptotic and cytotoxic effects of TP-Exos on ovarian cancer cells are somewhat weaker than those of free TP, TP-Exos displays a significantly stronger inhibitory effect on cancer cell growth and proliferation. However, it's worth noting that TP-Exos has certain toxic effects on the spleen and liver, necessitating further optimization to mitigate these effects. Nevertheless, TP-Exos holds promise as a potential treatment for ovarian cancer[62].

Moreover, cisplatin-based chemotherapy is the primary treatment for ovarian cancer patients, but resistance to cisplatin often develops during treatment, leading to poor prognosis. Studies have revealed that both microRNA-497 (miR497) overexpression and TP can effectively target cisplatin-resistant cell lines by inhibiting the mTOR pathway. However, miR497 has limitations such as low transcriptional efficiency, unstable chemical properties, and poor water solubility, while TP is associated with systemic toxicity.

To address these challenges, researchers have developed exosome NPs (miR497/TP-HENPs) capable of co-delivering miR497 and TP. The results demonstrate that these nanoparticles are specifically enriched and collected by cancer cells. They promote the dephosphorylation of the over-activated PI3K/AKT/mTOR signaling pathway, induce the generation of reactive oxygen species, and upregulate the polarization of macrophages from M2 to M1. These effects facilitate cancer cell apoptosis and exhibit significant anticancer activity without any adverse effects *in vivo*. Therefore, miR497/TP-HENPs represent a promising approach to overcoming cisplatin resistance in ovarian cancer[63–65].

## 6. Conclusions

The therapeutic efficacy of TCM is primarily attributed to its active components, which can be classified into categories such as sesquiterpenoids, terpenoids, polysaccharides, saponins, alkaloids, and glycosides based on their chemical structures. However, some of these active ingredients may have limitations in clinical use due to their short plasma half-life, low solubility, and poor bioavailability. To address these shortcomings, nanotechnology has been increasingly applied in the clinical treatment of TCM, enabling the development of nano-targeted drug delivery systems that significantly enhance the clinical value of TCM in cancer treatment and prevention. Nevertheless, current research on the anticancer-active ingredients of TCM

primarily focuses on individual components. Most TCM-based anticancer nano-drug delivery systems are designed around a single active ingredient. There is still limited exploration of multi-component systems, which somewhat restricts the clinical efficacy and applications of TCM. The treatment of malignant cancer has shifted toward molecular targeted therapy, but malignant cancers often result from the complex interplay of multiple factors, pathways, and targets. Achieving a cure for cancer by solely blocking a single receptor or pathway is challenging.

TCM often consists of various effective components that exert a multi-pronged, multi-target effect. However, the composition of TCM is intricate. As research methods, theories, and technologies related to nano delivery systems and TCM continue to advance, it's essential to apply TCM theory, including the principles of TCM syndrome differentiation and channel reduction theory, in conjunction with modern perspectives on multi-target cancer treatment. Moreover, greater emphasis should be placed on combination therapy using multi-component TCM nano-drug delivery systems with improved biocompatibility, higher stability, and enhanced tissue targeting. This approach can unlock more clinical potential in the field of TCM cancer treatment.

It's important to note that in drug combination therapy, there are three possible interactions: synergistic, additive, and antagonistic. A rational drug combination can not only produce synergistic effects but also reduce the risk of drug resistance and adverse reactions. However, when the interactions between drugs are not well understood, blind combination therapy may not achieve the desired efficacy and can even lead to reduced effectiveness, increased toxicity, or drug-related issues. Therefore, careful consideration of the order and proportion of different drugs used is crucial in combined drug therapy.

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# 纳米靶向递送系统在中药抗肿瘤中的应用进展

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**摘要:** 肿瘤已成为仅次于心脑血管疾病死亡率第二高的疾病, 中药也因其治疗效果强、副作用少、靶点多已成为抗肿瘤主要的替代药物之一, 可在肿瘤治疗的不同阶段均发挥着重要作用。但由于中药溶解度差、渗透性差、消除快、稳定性差、生物利用度低、半衰期短等问题阻碍了其临床应用。为了克服中药抗肿瘤的局限性, 近年来, 纳米技术被用于中医的临床治疗。纳米靶向给药系统通过与中药有效成分在抗肿瘤中的结合, 使得中药纳米靶向给药系统在肿瘤治疗中发挥着越来越重要的作用, 部分中药纳米药物载体已进入临床试验或用于疾病诊断和治疗, 促进了中医药的发展。因此, 本文就纳米靶向递送系统在中药抗肿瘤治疗中的应用进展进行综述。

**关键词:** 纳米靶向给药系统; 中药; 肿瘤