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Research progress of curcumin and its nanodelivery system in anti-tumor field

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Abstract. The focus of attention these days is on cancer prevention and treatment, as it is the second leading cause of death worldwide and its incidence continues to rise year. Due to its interactions with different cells and molecules, curcumin, a polyphenol natural substance derived from the turmeric plant, has numerous important applications in malignant disorders. Curcumin has demonstrated a high usage value and important benefits in the treatment of tumors; however, it has certain drawbacks, including low solubility, poor targeting, fast metabolism, and poor stability. The goal of this article is to enhance curcumin's bioavailability and enhance the therapeutic impact of various tumor illnesses by means of a cooperative nano-drug delivery system involving chemotherapeutic medicines and curcumin.

Keywords: curcumin, nano delivery system, anti-tumor therapy

1. Introduction

As the world's greatest cause of mortality, cancer poses a serious threat to public health [1]. Statistics show that in 2022, there were around 20 million new instances of cancer and 9.7 million cancer-related fatalities [2]. Traditional Chinese Medicine-combination therapy is a new treatment approach and an important cancer treatment strategy as it shows promising anti-tumor potential [3]. Curcumin is a natural polyphenol component from turmeric root, the main bioactive component of turmeric spice, in the diketone group [4]. Curcumin has a wide range of pharmacological activities, such as antimicrobial, anti-tumor, anti-inflammatory, antiviral, and antifungal qualities. It also plays a variety of roles in regulating enzymes, adhesion molecules, transcription factors, protein kinases, cytokines, and REDOX balance involved in inflammation [5].

In recent years, curcumin in the field of anti-tumor research has been more and more in-depth, according to the horizontal molecular experiments related studies show that curcumin's main anti-tumor mechanism is to increase the target of tumor cells to drugs, regulate the transduction of proliferation and apoptosis signaling pathways and the expression of related enzymes, proteins and genes. Curcumin has a lot of potential, however its bioavailability is limited due to its low water solubility and quick bodily degradation. Numerous nanoformulations have been developed as a result of recent advancements in nanotechnology to solve these pharmacokinetic restrictions. [6], such as nanotechnology-based systems, liposome encapsulation designed to enhance their absorption and efficacy [7].

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2. Curcumin nanodelivery systems

2.1. Nanoparticle

Lipid nanoparticles, which are nanoparticles constructed using phospholipids or phospholipid derivatives [8], are the basic building blocks of nanotechnology and vary in size between 1 and 100 nanometers [9]. Many organic nanoparticles have been designed as curcumin delivery vehicles as anti-cancer therapy alternatives because of the advantages of nanoparticle administration, including biocompatibility, decreased toxicity, enhanced permeability and retention (EPR) effects, and precision targeting [10]. To improve the drug loading capacity, Guo et al. designed a REDOX-responsive lipid prodrug C210 nanoparticle delivery system to form nanoparticles with high drug loading capacity, which can improve the bioavailability and anti-tumor activity of curcumin derivative C210 [11]. Liu et al. prepared the early irinotecan hydrochloride-curcumin nanosystem (SICN). SICN is a promising carrier-free nanoparticle. When exposed to the acidic environment of tumors, SICN showed stronger cytotoxicity due to charge conversion, opening new ideas for combination therapy of tumors [12]. Li et al. designed a core crosslinked nanoparticle (CCL NPs). The results show that CCL NPs with surface-modified antibodies can actively target tumor cells, and the tumor inhibition rate is as high as 78.7% in vivo experiments. This work provides new ideas for the design of nanomaterials targeting breast cancer [13].

2.2. Liposomes

The liposome is a double-layer vesicle composed of phospholipids [14], with an aqueous core inside, which can encapsulate up to two therapeutic agents, and has high stability and efficient drug loading capacity [15]. At the same time, the liposome can be functionally modified to make it have specific recognition functions such as targeting [16]. Alharbi et al. designed exosomes and liposomal nanocarriers of mangiferin and curcumin, targeting the PI3K/Akt/mTOR pathway, protecting the compounds from degradation, allowing controlled release and improving cellular uptake to enhance drug delivery [17]. Liu et al. prepared FC-DP-LIP containing curcumin and 5-fluorouracil by thin film water method. It had good morphology, stability and drug encapsulation rate, showed good biocompatibility and was cytotoxic to a variety of cancer cells [18]. Li et al prepared novel liposomes (CUR-APR/HA&GA-LPs) modified with hyaluronic acid (HA) and glycyrrhizin (GA) for co-delivery of Aprepitan (APR) and curcumin (CUR) and induction of tumor cell apoptosis using CUR. The results showed that CUR-APR/HA and GA-LPs can inhibit tumor proliferation and metastasis, reduce extracellular matrix (ECM) deposition and tumor angiogenesis, and have a good anti-liver cancer effect [19].

2.3. Polymer micelles

Micelles are formed by self-assembly of an amphiphilic polymer at a critical micellar concentration (CMC), with a hydrophobic tail and a hydrophilic head [20]. Micelles not only increase the solubility of hydrophobic drugs, but also increase their biocompatibility, prolong the circulation in vivo and prevent the rapid breakdown of drugs [21], showing good prospects in tumor therapy [22]. Zhou et al. prepared multi-pH-sensitive polymer-drug conjugate mixed micelles, which can effectively co-deliver doxorubicin and curcumin, which can greatly reduce the side effects of doxorubicin, and have synergistic enhanced anti-tumor and anti-metastasis effects [23]. Liu et al. synthesized a novel REDOX-responsive mPEG-SS-PLA (PSP) polymeric micelle for the delivery of sorafenib (SAF) and curcumin (CUR). The study showed that mPEG-SS-PLA polymer micelles loaded with SAF and CUR showed enhanced therapeutic effects on hepatocellular carcinoma in both in vitro and in vivo models and had broad application prospects in cancer therapy [24].

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3. The application of curcumin in the field of anti-tumor

3.1. Breast Cancer

Breast cancer (BC) has become the fifth most common cause of cancer-related morbidity. Worldwide, breast cancer accounts for approximately 30% of cancers in women, with a mortality to morbidity ratio of 15% [25]. The researchers found that BC can be fought with a curcumin nanodelivery system [26]. Lv et al. synthesized a curcumin-carrying polymer nanocarrier (HA-b-PCDA). Molecular docking and molecular dynamics studies showed that these drug-carrying HA-b-PCDA nanoparticles significantly inhibited the proliferation and stem cell formation of BCSC-rich 4T1 mammary spheres, and could deliver a variety of clinical chemotherapy drugs [27]. Novel core-shell nanoparticles with controlled release properties for zinc ions and curcumin were successfully created by Gao et al. The amounts of ZIF-8, CUR, SF, and PDA in a hybrid nanoplatform were carefully controlled for the first time using microfluidic fast mixing to enhance anti-cancer efficacy [28].

3.2. Lung Cancer

Lung cancer is the most common cancer globally in terms of diagnoses [29], accounting for 1.79 million deaths and 2.2 million new cases yearly, making it the leading cause of cancer-related death globally [30]. Radiation therapy, chemotherapy, targeted therapy, and surgical excision are the current therapeutic approaches. Even though other EGFR tyrosine kinase inhibitors (EGFR-Tkis) have been developed, such as erlotinib (Er), acquired resistance to these medications presents a major challenge and lowers their long-term effectiveness in treating lung cancer [31]. As a result, curcumin nanodelivery technologies present an innovative therapeutic strategy. Chen et al. combined Er with curcumin (Cur), an important ingredient in traditional Chinese medicine, to improve the treatment's effect on lung cancer. By preserving the level of ikappa-B expression and suppressing the production of PI3K in the EGFR downstream signaling pathway, Cur can prevent Er resistance by preventing the growth of tumors. Sasikarn Sripetthong developed curcumin-loaded nanomicelles using quaternium-salt chitosan and vanillin imide (QCS-Vani) conjugates as carriers and investigated their entrapment rate. According to the study, curcumin-loaded QCS-Vani nanomicelles triggered apoptosis in lung cancer cells and shown better cytotoxicity and selectivity against the lung cancer A549 cell line and decreased toxicity against normal cells (H9C2) [32].

3.3. Liver Cancer

Liver cancer, particularly hepatocellular carcinoma (HCC), is a major global health problem due to its high prevalence in many countries [33]. The high mortality rate of HCC should be attributed to late diagnosis and limited treatment. Drug therapy is a common palliative strategy for clinical treatment. However, they have many disadvantages such as low selectivity, dose restriction, toxicity, and adverse side effects [34]. Therefore, identifying new, effective codosing system dosage forms remain an important research focus. The use of lipid nanoparticles as delivery vehicles for insoluble medications like curcumin has been investigated. According to Wei et al., curcumin-human serum albumin nanoparticles modified with a peptide that binds to programmed death ligand 1 (PDL1) can enhance the delivery of drugs targeted at tumors while also reestablishing the immune system by preventing the PDL1/PD1 connection and coordinating anti-cancer efforts. [35]. Curcumin/triphenylphosphine bromide chitosan-G-poly (TPP-CZL) nanomicelles have been shown by Li et al. to significantly reduce mitochondrial membrane potential, increase the expression of pro-apoptotic protein Bcl-2, decrease the expression of anti-apoptotic protein Bax, and promote apoptosis in liver cancer cells based on cell survival rate and Hoechst staining results [36].

4. Summary

Because they are safe and effective, researchers are considering the use of natural compounds as potential chemotherapeutic medicines. The active hydrophobic polyphenol curcumin, which is derived from the rhizome of the turmeric plant, has demonstrated promise as a cancer treatment. We have been

obliged to refocus our attention from a single target to the regulation of the body's network due to the substantial obstacles presented by cancer, as well as the bad responses and drug resistance brought on by prolonged therapy with a single agent. The emergence of nanobiotechnologies has further opened vast opportunities to explore and expand the use of curcumin in the medical field. Nanodelivery systems using curcumin and its derivatives have better bioavailability and solubility, have clear advantages in anti-tumor therapy, and can deliver drugs to different targets or sites of action. As reported in this review, the curcumin nanodelivery system has attracted much attention, which will become a new method of cancer treatment, and it is believed that curcumin will have more extensive and important applications in the anti-tumor field in the future.

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