Liposomes: A Highly Efficient and Reliable Nanocarrier For The Treatment Of Breast Cancer And Lung Cancer

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Abstract. Cancer is one of the diseases with the highest mortality rates in the world today, and cancer itself is very difficult to treat. Among these, breast cancer and lung cancer are exceptionally severe types of cancer. The complexity, heterogeneity, drug resistance, and immune evasion of cancer present enormous challenges for doctors and scientists. In recent decades, scientists have explored various methods to tackle cancer. Although progress has been made, treating cancer remains challenging. Using nanocarriers to deliver drugs for targeted therapy is an effective treatment method. However, nanoparticle-based drug therapies encounter issues such as targeting selectivity, biocompatibility, and safety concerns. Liposomes, a type of nanocarriers encased in lipid bilayers that encapsulate pharmaceuticals, exhibit their advantages among a plethora of carriers. Liposomes possess characteristics such as multiple targeting capabilities, high bioavailability, and elevated safety. At present, it has emerged as a nanocarrier for combating various cancers, including breast cancer and lung cancer. This article will focus on the characteristics of liposomes and their therapeutic efficacy in the treatment of lung cancer and breast cancer.

Keywords: Liposomes; Breast cancer; Lung cancer; Nanocarrier.

1. Introduction

Cancer is regarded as one of the most dreaded afflictions of the 20th century and its prevalence continues to rise into the 21st century. Annually, there are more than 14 million new cases worldwide, with over 1.1 million cases reported each year in India. Cancer originates from aberrant cellular proliferation, during which cancerous cells lose their capacity to cease growth. Cancer cells also have invasiveness and metastasis. They not only invade and destroy surrounding normal tissues, forming invasive tumors but can also detach from the primary site and spread through blood or lymphatic systems to other parts of the host, forming new tumors. It can commence in any organ or bodily structure and typically must reach a size of 1 centimeter or comprise 1 million cells before it becomes detectable [1]. Breast cancer stands as the most prevalent non-skin malignancy among women, with one in eight women receiving a diagnosis of this disease during their lifetimes. The five-year survival rate for patients diagnosed at an early stage is an impressive 98%, whereas it drops to 72% for those with stage III and diminishes further to 22% for stage IV [2,3]. Lung cancer is also a common type of cancer. Its early symptoms are not obvious, and it is easily transferable. Combined with the large number of smokers worldwide, lung cancer affects a significant number of people, and these characteristics make it the leading cause of cancer deaths. Since early-stage cancer is much easier to treat compared to late-stage cancer, we must find ways to conduct targeted treatment as soon as possible. The current treatment methods for cancer mainly include surgery, radiation therapy, chemotherapy, targeted therapy, and so on. Despite the many treatments available, cancer remains extremely difficult to cure. Using nanocarriers to deliver drugs is also a better method for targeted therapy. Among them, liposomes are a very promising type of nanocarrier. Liposomes are tiny vesicles composed of lipid bilayers, structurally similar to cell membranes. Liposomes can be used to encapsulate drugs to protect their stability within the body and effectively transport them to specific locations. Liposomes possess numerous characteristics, including a robust capacity for targeted delivery, multiple targeting possibilities, low toxicity, and excellent biocompatibility. In terms of targeted delivery, liposomes can utilize their surface modification capabilities to target specific cells or tissues. For instance, liposomal cancer drugs can increase the selectivity of the drug for tumors by

targeting receptors that are unique to tumor cells. Moreover, the anticancer agent Doxorubicin, encapsulated in liposomes, forms Doxil. This liposome-encapsulated formulation significantly mitigates the drug's toxicity while enhancing its concentration within tumor tissue, thereby augmenting its therapeutic efficacy. To further enhance the use of liposomes in cancer treatment, scientists have conducted a variety of theoretical studies and clinical trials. Therefore, this article seeks to explore the instances and potential of utilizing liposomes for the treatment of breast cancer and lung cancer.

2. Liposome

2.1. The concept of liposomes.

Liposomes are small vesicles composed of lipid bilayers, resembling the structure of cell membranes. Typically formed spontaneously by lipid molecules such as phospholipids and cholesterol, they encapsulate an aqueous solution within. The essence of a liposome is characterized by one or more concentrically arranged lipid bilayers encompassing one or more aqueous compartments. Owing to their structural similarity, liposomes serve as carriers for pharmaceuticals, enclosing drugs within their interior, and facilitating targeted delivery to specific sites within a biological organism via natural pathways [4]. This mode of delivery enhances the bioavailability of medications while minimizing toxic side effects on non-target tissues, thereby improving therapeutic efficacy.

Liposomes boast a broad spectrum of applications in areas such as drug delivery, gene therapy, cosmetics, food, and medical research. They are particularly prevalent as drug carriers within the realm of nanoparticle-mediated drug delivery. In contemporary clinical studies, liposomes have been employed in the treatment of various conditions, including breast cancer, ovarian cancer, and lung cancer [5].

Furthermore, the size, composition, and preparation methods of liposomes can be tailored to meet specific application requirements, optimizing their performance and stability within biological systems.

2.2. The mechanism of action of liposomes.

On one hand, Liposomes are made up of a phospholipid bilayer with distinct hydrophobic and hydrophilic areas. This unique structure enables them to trap drug molecules in the hydrophobic core of the membrane or to hold water-soluble drugs in the surrounding aqueous environment. By forming one or more sealed compartments, liposomes effectively encase drugs, shielding them from degradation in the body and enhancing their stability and effectiveness. On the other hand, liposomes, especially those containing the bioreductive component SS14, are designed by scientists to facilitate DNA release and transfection. SS14 is a reductively sensitive double-chain surfactant that can undergo depolymerization in reductive environments (such as inside cells), thereby promoting liposome disassembly and DNA release [6].

2.3. The advantages of using liposomes.

Liposomes represent a meticulously studied class of nanoparticles that confer a multitude of advantages. Functionally, they are capable of stably encapsulating drugs, thereby mitigating drug degradation. Liposomes can encapsulate both hydrophilic and lipophilic medications, and by modulating lipid composition and fabrication processes, the encapsulation efficiency for various types of drugs can be significantly enhanced. Furthermore, they can improve pharmacokinetics by prolonging the drug's retention time within the body, while effectively reducing the frequency of administration [7]. Additionally, liposomes can adeptly surmount significant barriers, such as the blood-brain barrier and cell membranes, facilitating the delivery of therapeutic agents to targeted sites. Lastly, liposomes are particularly beneficial for drugs that possess a narrow therapeutic window or

target resistant pathogens, offering an alternative formulation for those medications that exhibit limited efficacy or are challenging to manage with traditional preparations.

Compared to other nanocarriers, liposomes are relatively convenient to prepare, with their manufacturing processes being relatively mature. Common methods such as the thin-film hydration technique and sonication are suitable for large-scale production. Secondly, liposomes exhibit multifunctionality; they can be combined with other nanomaterials to create multifunctional carriers that enable combined therapeutic and diagnostic purposes. Lastly, liposomes can effectively enhance biodistribution; they alter the biodistribution of drugs, increasing the accumulation of drugs in target tissues and thereby enhancing therapeutic efficacy.

2.4. Classification of liposomes

There are many types of liposomes, and they can be divided in various ways from different perspectives. Based on the structural classification, liposomes can be divided into unilamellar liposomes and bilamellar liposomes. charge properties, liposomes can be classified into neutral liposomes, cationic liposomes, and anionic liposomes. Cationic liposomes can bind to negatively charged nucleic acid molecules, enhancing delivery efficiency. They are chiefly utilized for gene delivery and intracellular transport, finding extensive applications in the realms of gene therapy and vaccine delivery. While anionic liposomes can be used for delivering positively charged drugs. They are primarily employed for the delivery of negatively charged pharmaceuticals or nucleic acids, engaging in interactions with immune cells. Based on the particle size, they can be classified into small liposomes, medium-sized liposomes, and large liposomes. Among them, small liposomes typically have a diameter ranging from 20 to 100 nanometers, while medium liposomes have a diameter of approximately 100 to 500 nanometers. Large liposomes possess a diameter exceeding 500 nanometers. The varying sizes of liposomes facilitate the selection of therapeutic approaches, thereby enhancing the feasibility of treatment.

Based on the development history of liposomes, they can be categorized into the following types: Conventional liposomes are the earliest developed and utilized liposomes, primarily used for drug delivery. Generally, they are composed of natural or synthetic phospholipid bilayers and are often spherical or vesicular in shape, designed for the delivery of chemotherapy drugs and antibiotics. Subsequently, in the 1970s, PEG-coated liposomes emerged. These liposomes were modified by attaching polyethylene glycol (PEG) chains to their surface. The hydrophilic nature of PEG reduced protein adsorption on the liposome surface, enabling better evasion of the immune system and facilitating the delivery of drugs to their designated targets. Later on, a more diverse range of liposomes with distinct properties emerged, such as magnetic liposomes, ligand-targeted liposomes, enzyme-triggered liposomes, and so on. The remarkable efficiency and specificity of liposomes render them an object of intense fascination for scientists. Over recent years, a plethora of innovative liposome variants has surfaced, including photothermal therapy liposomes. These liposomes harness photothermal agents, such as gold nanoparticles, capable of transforming near-infrared light into thermal energy, thereby inducing localized hyperthermia and eradicating adjacent cancer cells. This technology holds immense promise as a highly beneficial nanocarrier for the future of cancer treatment. The diversity of liposomes ensures their multifunctionality, strong targeting ability, and high biocompatibility (**Fig. 1**).

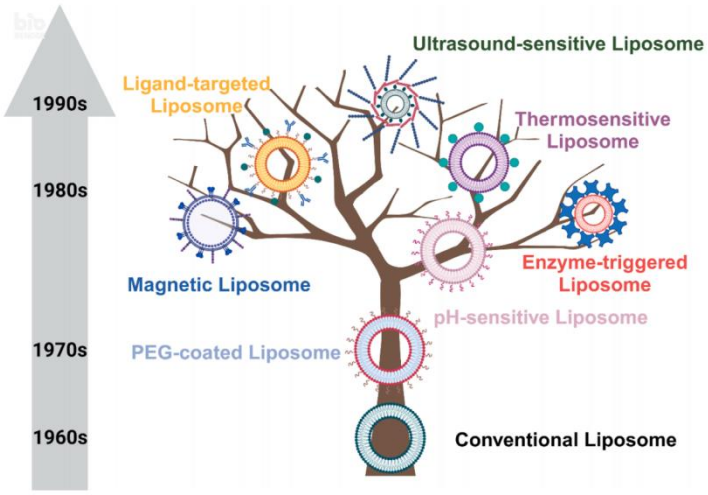

Fig. 1. The evolution of the discovery, development, and types of liposomes [8].

3. The utilization of liposomes in cancer treatment

3.1. Breast cancer

Breast cancer is a typical cancer among women, while it occurs less frequently among men. The principle of breast cancer is the abnormal proliferation of cells in the breast, leading to the formation of a tumor. Despite the availability of more treatment options and advanced treatment methods now, breast cancer is still one of the high mortality cancers. At present, the severity of breast cancer is reflected in its complex biological characteristics, stem cell-driven invasiveness, and resistance to many existing treatments [9]. Breast cancer encompasses various subtypes, each exhibiting intricate biological characteristics that complicate the pursuit of personalized treatment. Furthermore, many patients with breast cancer develop resistance to therapeutic agents, resulting in suboptimal treatment outcomes. The liposome technology discussed in this article has made some progress in the treatment of breast cancer. For example, there are drugs encapsulated in liposomes, such as liposomal doxorubicin (Doxil), which have been used in the treatment of breast cancer and have shown very promising results.

3.1.1 The process of treatment

Liposomes are highly effective as nanocarriers due to their unique properties and specialized drug delivery systems, allowing for precise targeting of tumor sites. Upon reaching these locations, they release their payload, which disrupts the growth and division of cancer cells through its specific mechanism, thus accomplishing the intended therapeutic outcomes. Liposomes play a key role in drug delivery for breast cancer treatment through a few different methods [10]. First, there is passive targeting. Given their size (around 100 nanometers) and the tendency for blood vessels in tumors to be leaky, liposomes tend to accumulate naturally in cancerous or inflamed tissues. The second method is active targeting. By attaching specific ligands to their surface, liposomes can actively seek out and bind to breast cancer cells. This strategy boosts the concentration and effectiveness of the liposomes in tumor sites by interacting with specific receptors on the cancer cell surfaces.

3.1.2 Current drugs

In recent years, the use of liposomes in clinical trials for breast cancer treatment has emerged as a vital research area. Significant advancements have been observed, particularly with liposomal formulations like Doxil (a liposome-encapsulated version of doxorubicin), which has shown encouraging outcomes, especially in advanced breast cancer cases. Furthermore, researchers are exploring new liposome types, such as self-assembling and multifunctional variants. These cutting-edge liposomes may provide benefits like enhanced drug loading capacity, prolonged circulation times, and improved targeting efficiency. Doxil, a liposomal formulation of doxorubicin, is

particularly utilized for treating advanced breast cancer, especially in patients resistant to conventional chemotherapy. The mechanism is intriguing: by encasing doxorubicin within liposomes, it minimizes toxicity to healthy tissues while enhancing the targeting precision and effectiveness of drugs.

3.2. Lung cancer

Lung cancer poses a severe challenge to global health, standing as one of the most prevalent malignancies worldwide. The incidence and mortality rates associated with lung cancer are particularly alarming, with millions of new cases and deaths reported annually. These statistics vary by region, influenced by local smoking habits, air pollution, the availability of medical resources, and the accessibility of early detection and treatment. Currently, North America, Western Europe, Eastern Europe, and certain regions of Central Asia exhibit a higher incidence of lung cancer, largely correlated with elevated smoking rates. Despite advancements in lung cancer treatment in recent years, including the development of targeted therapies and immunotherapies, the efficacy of these treatments varies among patients due to individual differences. Furthermore, the subtlety of early symptoms often leads to patients being diagnosed at advanced stages, complicating treatment and resulting in lower survival rates. Therefore, enhancing the efficacy of lung cancer treatment remains a significant objective, with liposomes potentially playing a pivotal role in this endeavor.

3.2.1 The process of treatment

Liposomes offer significant support in the treatment of lung cancer, encompassing a multifaceted role in targeted delivery, enhancing drug bioavailability, minimizing side effects, augmenting penetration capabilities, combinatorial therapy, and gene therapy. These benefits render liposomes a promising drug delivery system that aids in enhancing the efficacy and safety of lung cancer treatment. The structure of liposomes facilitates the traversal of biological membranes, including the lung's blood-gas barrier and cellular membranes, thereby improving the efficiency of drug delivery to cancer cells within the lungs. Particularly for situations requiring localized drug release within the lungs, liposomes provide an effective route for drug delivery. Liposomes can also be employed in gene therapy to deliver genetic drugs (such as siRNA, mRNA, or DNA) to lung cancer cells, thereby inhibiting oncogene expression or repairing mutated genes. This approach offers a high degree of specificity and potential therapeutic efficacy. These are the advantages of using liposomal therapy for the treatment of lung cancer [11].

3.2.2 Research Progress

In contemporary times, the therapeutic approaches for lung cancer encompass surgical resection, radiation therapy, chemotherapy, targeted therapy, and immunotherapy, among others. The selection of a treatment regimen is contingent upon the staging of the tumor, the nature of genetic mutations, and the physiological condition of the patient. In recent years, the field of lung cancer treatment has witnessed remarkable advancements, particularly in the realms of genomics, molecular biology, and immunotherapy. These breakthroughs have opened new avenues for the early detection of lung cancer and the development of personalized therapeutic strategies.

In the scientists' previous experiments, they used TPP-LND@Lip, a type of liposome, which slowed down mitochondrial oxidative phosphorylation (OXPHOS) and reduced PD-L1 expression in tumor cells. This significantly alleviated the hypoxic condition in lung cancer tumors, thereby enhancing the effectiveness of radiotherapy. Liposomes have the ability to suppress PD-L1 expression. The LND contained in liposomes can reduce PD-L1 expression both within and on the surface of lung cancer cells by activating the AMPK pathway. This decreases immune tolerance and increases sensitivity to radiotherapy [12]. Currently, there is a drug encapsulated in liposomes—Liposome-encapsulated Paclitaxel (LipoTaxol)—undergoing clinical trials. This formulation aims to enhance the bioavailability of paclitaxel and mitigate its toxic side effects. The clinical trials are assessing its efficacy against non-small cell lung cancer [13].

4. Some Challenges and Prospects for the Future

As noted previously, liposomes present considerable benefits in the treatment of lung and breast cancer. Nevertheless, their future development is encumbered by certain drawbacks, such as elevated manufacturing costs and challenges with liposome stability. Despite the hurdles encountered in the clinical application of liposomes, this should not lead to a pessimistic view regarding their overall potential. In stark comparison, scientists maintain an optimistic perspective on the future of liposomes. Advancing in tandem with the continuous ascent of nanotechnology, the judicious employment of liposomes could potentially proffer a multitude of novel prospects for augmenting therapeutic efficacy and mitigating ancillary effects. Presently, the People's Republic of China has ratified the usage of three variegated liposomal entities (notably, Lipusu, doxorubicin encapsulated within liposomal confines, and amphotericin B similarly encased), and both behemoth pharmaceutical entities and fledgling innovative firms within China are currently in the throes of devising nanomedicines, including but not limited to liposomes. The National Medical Products Administration (NMPA) has also accorded preeminent significance to the "safety and quality assessment of nanomedicines" as a cardinal project and is in the nascent stages of devising a regulatory backdrop that is both fluid and comprehensive for the advent of nanomedicines to come [14]. Recent achievements indicate that liposomes, with their numerous advantages, play a significant role in targeted drug delivery.

5. Conclusion

In contemporary society, breast cancer and lung cancer pose significant threats to human health. The primary reason for this is that current treatment modalities are insufficiently effective in managing these two cancers. However, the advent of liposomal technology holds promise for advancing new therapeutic approaches in this domain. Overall, liposomes are a very promising nanocarrier in the treatment of lung cancer and breast cancer. It has many advantages and features. Compared to other nanoparticle carrier technologies, liposomes have the advantages of multiple targeting, high bioavailability, stability, and fewer side effects. It is capable of delivering medication with remarkable efficiency to the designated site, enabling effective targeted therapy for tumors. A vigorous advancement in liposome technology could provide a novel and effective avenue for the treatment of cancer. Scientists believe that in the future, with further advancements in nanotechnology research, liposomes may be capable of treating these two types of cancer.

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