Research of Nanoparticle Drug Delivery System of Breast Cancer

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Abstract. This passage talks about the formation of breast cancer and the traditional treatment of curing breast cancer. Breast cancer is one of the most common cancers all over the world. There are many people died because of this cancer. Now, doctors have several methods to cure this cancer, and the two most common methods are radiation therapy and surgery. Although these methods can cure breast cancer, they have several disadvantages and scientists try to find new ways to cure breast cancer. With the invention of technology, scientists invented the nanoparticle drug delivery system and tried to use nanoparticle drug delivery systems to treat breast cancer. Nanoparticle drug delivery systems also have different ways and limitations in curing breast cancer. The passage talks about three main ways: Liposomal nanoparticles system, Polymer-based nanoparticles system, and Superparamagnetic iron oxide nanoparticles system.

Keywords: Breast cancer; Radiational therapy; Surgery; Nanoparticles drug delivery system.

1. Introduction

Cancer, a common disease in our world, has many kinds of cancer. Different kinds of cancer have many different symptoms. Breast cancer is a kind of cancer and it's a prevalent cancer in the world. In America, there are about 19.8 women died because of breast cancer in every 100,000 in 2018.

It's the second-largest death rate in 2018. In 2020, there are 2.3 million people who have breast cancer worldwide. Although doctors and scientists make many remarkable advances to cure cancer, the therapy methods are not curative. Cancerous cells grow multiply and become tumors in women's breasts. Then those cancerous cells will spread from your breast to other areas of your body. There are also different kinds of breast cancer in the world, and there are about six common kinds of breast cancer worldwide. There are five stages of breast cancer. Like cancers, breast cancer also has several subtypes. Bacteria evolved several years and scientists found the most common breast cancer subtype is based on estrogen (ER), progesterone (PR), and **human epidermal growth factor 2** (HER2). These subtypes are the LUMINAL A subtype, LUMINAL B subtype, HER2 subtype, and TNBC subtype. There are also several stages of breast cancer. Breast cancer is divided into five stages. Stage 0 is the easiest, stage I and II are early-stage inventions. In stage III, bacteria begin to spread, and bacteria begin to spread into other tissues in the body in stage IV [1].

Breast cancer has many different causes. According to the research, women are more likely than men to get breast cancer. The other main factors are increasing age and family history. If a person has a family history of breast cancer, she may have a high risk of getting this disease. Other factors like drinking alcohol and radiation exposure lead people to get breast cancer as well. When there is a mass or area of thickened skin in the breast that has a different texture from the surrounding area, a nipple that appears sunken or is pulled towards the chest, discoloration of the breast skin, and variations in the breast's dimensions, form, or overall look, people may get breast cancer. Signs of breast cancer also have alterations to the breast skin, such as a pitted texture like an orange peel [2].

Because cancer is a very big problem all over the world, many cancers find the factors that cause them. Breast cancer is one of those cancers; Scientists don't find the exact causes factor of breast cancer. The causes of breast cancer are genetic problems and environmental problems. When people have breast cancer, they will feel a tumor in the breast, and the bacteria will spread to other parts of their bodies. When the bacteria spread, this will be called metastatic cancer instead of breast cancer.

Breast cancer often starts due to genetic mutations in the cells that line the milk ducts. These ducts are the channels that carry milk to the nipple. Cancer that begins with the ducts is known as invasive ductal carcinoma. It's also possible for breast cancer to develop in the lobules, which are the glands responsible for milk production. When this happens, cancer is called invasive lobular carcinoma. Although it's less frequent, breast cancer can originate from other types of cells within the breast as well. Various risk factors may increase the likelihood of developing breast cancer, such as having a family history of breast cancer, drinking alcohol, getting older, and other elements that contribute to the risk (Figure 1).

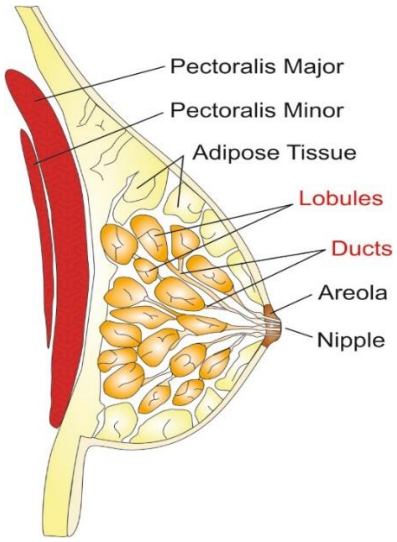

Fig 1. The formation of breast cancer [3].

Because breast cancer is dangerous and has a high morbidity, scientists make many efforts to find better treatment. Now, people have 6 different methods to treat breast cancer. These methods are surgery, radiation therapy, chemotherapy, hormone therapy, targeted therapy, and Immunotherapy. Although traditional methods have advantages and are useful, these methods have some drawbacks and side effects. Radiation therapy and surgery are two common therapies. Radiation therapy may cause radiation dermatitis, myelosuppression, radiation lung injury, radiation cardiac injury, feeling tired, and edema of the arm. Based on technological innovation, radiation therapy can treat cancer bacteria more precisely. Patients should communicate with doctors to minimize these side effects. Surgery has some risks to recrudescence. Patients need to have other methods to assist with surgery. Patients need to have several surgeries to cure breast cancer. Postoperative complications may happen as well. Surgery may cause psychological changes, subcutaneous effusion, flap necrosis, upper limb edema, and edema of the arm [4].

Currently, people use chemical medicine to cure breast cancer. These treatments are because chemical medicine has some treatments that have long-term side effects. After the treatments, some serious side effects are Bone narrow problems, lung problems, and Blood clots. Except for serious side effects, there are also common side effects. The most common side effects are low red blood cell count and weakness. That means breast cancer can also cause ammonia. Immunotherapy for breast cancer can’t have obvious effects for all people. Some people have obvious effects by using immunotherapy and some people don’t have obvious effects. This method can cause overreaction after using immunotherapy. There are no biological markers of predictive immune checkpoint-blocking inhibitors. This inhibits the concise of immunotherapy. The cost of immunotherapy is also very expensive [5].

Doctors try to use nanoparticles to cure diseases. In curing breast cancer, nanoparticles have different ways due to the properties and sizes of nanoparticles. Nanoparticles can deliver the drug, imaging, overcoming drug resistance, breaking through biological barriers. Compared to these classic treatments, nanoparticle transport systems have several advantages. Scientists use nanoparticle-based platforms to help diagnose breast cancer. The platforms can overcome biological barriers and allow

prolonged blood circulation time, simultaneous tumor targeting, and enhanced accumulation of drugs in tumors [6] (Figure 2). There are many advantages of nanoparticle drug delivery. Nanoparticle drug delivery system can improve drug bioavailability which increases drug concentration and bioavailability in the body, enhances tumor targeting, reduces side effects, controls drug release, improves drug solubility, combines treatment strategy, improves the pharmacokinetic properties of drugs, enhances immunotherapy and enhances immunotherapy.

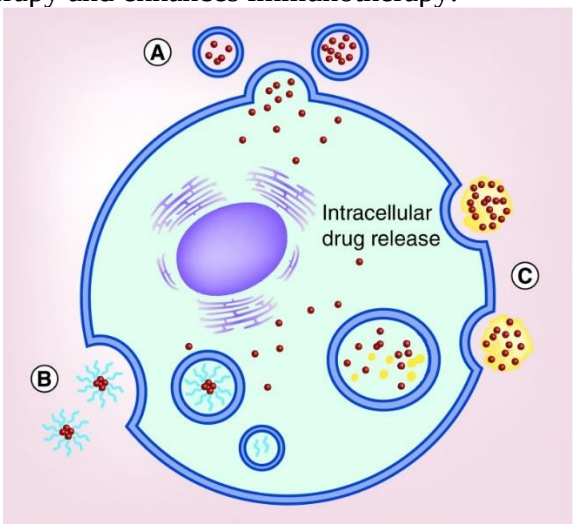

Fig 2. The spread of breast cancer bacteria [6].

2. Traditional treatments of breast cancer and nanoparticle drug delivery system

2.1. Challenges of Breast Cancer Treatment

To cure breast cancer, people need to find the subtypes of breast cancer. Different subtypes have different treatments. This step is the first step in curing cancer and it's the most important step. Breast cancer treatments need to be in good condition. Good conditions increase the cure for success of breast cancer. That makes poor places have a low success in curing breast cancer because these places have bad conditions. In stage 0 and stage I of breast cancer, people have a higher curing rate. Poor countries and places need to use limited sources to cure patients of breast cancer. The diagnosis of breast cancer's early stage isn't correct because of limited sources [7]. Breast cancer may recurrently after a long time. When patients have advanced breast cancer, the choices are very limited, and the prognosis is poor. Patients with advanced breast cancer only have a 20% survival rate at 5 years old.

How to choose the most effective therapy treatment is also a difficult point in curing breast cancer. Breast cancer cells can become resistant to certain treatments, especially for HER2-positive and HR-positive/HER2-negative breast cancer, where treatment resistance is an important challenge. Due to the low prevalence of breast cancer screening and patients' low awareness of the disease, the early diagnosis rate of breast cancer patients in China is currently low, and relatively many patients with middle and advanced breast cancer are diagnosed.

2.2. Cancer treatment

Breast cancer is a legal disease, and many women died of this. Many women died because of breast cancer. Scientists have found many ways to cure this disease. The most popular way to cure breast cancer is by adding several molecular markers such as miRNAs and mutations [8]. Although these ways are beneficial for patient's health, there are long-term effects. Patients have several other effects during therapy. These effects may cause other health problems. Although patients don't have breast cancer, they may have other bad health problems. Cancer viruses have a high proliferation rate. Also,

because of abuse of the traditional drugs, those drugs don't have the effects of killing the cancer virus. To decrease the side effects of the treatments, scientists try to use other ways to cure breast cancer.

In the first-line treatment of metastatic HER2-positive breast cancer, trastuzumab, in combination with chemotherapeutic agents, significantly improved patients' progression-free survival (PFS) and overall survival (OS). For example, in the CLEOPATRA trial, the treatment regimen of trastuzumab in combination with rituximab and docetaxel resulted in a median progression-free survival (mPFS) of 18.7 months and a median overall survival (mOS) of 57.1 months.

2.3. Basic information of nanoparticle drug delivery system

While finding other ways to cure breast cancer, people find that they need to treat the disease through genetics part or using other drugs that don't have many side effects on people's bodies. By finding nanoparticle materials, people find another way to treat breast cancer. The nanoparticle delivery system uses the nanoparticles to deliver drugs and control the release of **therapeutic agents. To cure the disease easier,** people **decided to use the nanoparticle system to cure the diseases.**

Nanoparticle drug delivery system using liquid-based drug delivery to transport the drugs to certain cells or tissues. Nanomedicine can improve drug stability, aqueous solubility, blood circulation time, controlled release, and targeted delivery at the tumoral site and enhance therapeutic safety and effectiveness. It has several benefits over traditional methods of curing breast cancer. Based on different degrees of breast cancer and subtypes, there are different transportation ways to deliver the drug. A nanoparticle delivery system can make it easier to target the organs or tissue. By nanomedicine, drugs reach the blood directly. The blood can absorb the drugs very rapidly and highly. Nanoparticle drug delivery systems have several different types.

Liposomal nanoparticles (LNPs) are spherical structures made up of phospholipid bilayers, which can range in size from tens to hundreds of nanometers. These vesicles have a hydrophobic lipid bilayer that encases a hydrophilic core, allowing for the encapsulation of both hydrophobic and hydrophilic therapeutic compounds. The hydrophobic drugs are typically embedded within the lipid bilayer, while hydrophilic drugs are housed in the core. This encapsulation process significantly minimizes the toxicity associated with drug off-target distribution. Furthermore, drugs with amphiphilic properties can be incorporated into the aqueous core of LNPs. These nanoparticles have a propensity to accumulate in tumor cells, leveraging the cell membrane-bound bilayers for delivery. The surface of LNPs can be modified with polyethylene glycol (PEG) to enhance their circulation time and targeting efficacy. PEGylated LNPs have demonstrated effective passive targeting in both in vitro and in vivo settings.

LNPs also facilitate the delivery of drug combinations by encapsulating multiple therapeutic agents, which can work synergistically. They have proven to be efficient carriers for various therapeutic molecules, including oligonucleotides, peptides, and siRNA-based gene therapies. By encapsulating these molecules within LNPs, they are protected from degradation in the bloodstream and can be delivered directly to their targets via specific ligands.

Polymer-based nanoparticles (PNPs) are colloidal particles that measure several hundred nanometers in diameter. They are generally synthesized by blending a copolymer with another polymer matrix. The polymers utilized can be naturally derived, such as cellulose and chitosan, or they can be synthetic polymers chosen for their specific chemical and biological properties. This versatility makes PNPs highly sought after for a variety of biomedical applications.

Common techniques for the chemical synthesis of PNPs include nanoprecipitation, emulsification, and salting out. These methods allow for the creation of PNPs with tailored lipophilicity, charge, and biocompatibility, which are essential for directing drugs to specific targets within the body. Anticancer drugs can be incorporated into the drug delivery system (DDS) of PNPs through surface adsorption, chemical coupling, or encapsulation. PNPs are known for their high solubility and permeability, which contribute to their stability and ability to release drugs slowly over an extended period. This makes them particularly effective as nanocarriers for anticancer drugs that are less hydrophilic. Moreover, research into PNPs extends beyond the delivery of traditional

chemotherapeutic agents, with investigations into various methods of cancer suppression to enhance their therapeutic potential.

There are many types of metal-based nanoparticle drug delivery systems, which are gold nanoparticle drug delivery systems, superparamagnetic iron oxide nanoparticle drug delivery systems, and quantum dots. The predominant method for producing gold nanoparticles (AuNPs) is through the reduction of gold ions (Au3+) by citrate in an aqueous solution. These nanoparticles are extensively utilized in drug delivery systems (DDS) due to their adjustable characteristics and minimal toxicity to cells. To ensure that drug delivery systems (DDS) can accurately target specific receptors or biomarkers, the application of organic coatings on the surfaces of gold nanoparticles (AuNPs) is essential. Sulfates and disulfides are often chosen for these coatings because of their exceptionally binding capabilities to gold surfaces. This allows for the subsequent attachment of drugs or therapeutic agents to the AuNPs via either covalent or non-covalent bonding methods.

In the realm of nanomedicine, superparamagnetic iron oxide nanoparticles (SPIONs), measuring 1 to 100 nanometers, are gaining attention. These nanoparticles feature a magnetic core composed of either magnetite (Fe_3O_4) or maghemite (γ-Fe_2O_3), with magnetite being the preferred choice due to its reduced toxicity. Despite its benefits, direct use of SPIONs can lead to biofouling and aggregation in plasma, which poses significant challenges. To mitigate these issues, the magnetic core of SPIONs is typically enclosed within a hydrophilic polymer coating, which not only stabilizes the nanoparticles but also facilitates the targeted delivery of biomolecules. Some of the most commonly employed biopolymers for this purpose include polysaccharides, polyethylene glycol (PEG), dextran, alginate, and polyacrylic acid.

The use of SPIONs as contrast agents in medical applications such as immunoassays, tissue repair, chemotherapy, and magnetic resonance imaging (MRI) is on the rise. Their natural biocompatibility and magnetic characteristics enable the guidance of therapeutic agents to precise locations within the body using external magnetic fields, thereby enhancing the visualization and effectiveness of treatments.

For cancer cell imaging, which is essential for monitoring tumor progression and drug effectiveness, quantum dots are valuable due to their superior optical characteristics. Quantum dots are semiconductor nanocrystals with sizes ranging from 2 to 10 nanometers. They typically consist of a metallic core that emits light across a narrow spectrum, from visible to infrared (IR) wavelengths. The quantum dots' outer shell can be composed of various doped metal or semiconductor materials, tailored to specific applications. The combination of quantum dots with surface-modified ligands and peptides enables their use in target-specific cancer research. Unlike other nanoparticles mentioned, quantum dots offer in vivo cellular imaging capabilities due to their tunable optical properties, large surface-to-volume ratio, high brightness, and resistance to photobleaching.

However, a significant challenge with quantum dots is their inherent hydrophobicity, which necessitates surface coating with polymers or multilayer ligand shells to enhance water solubility. Coating with PEG not only reduces the potential for toxic accumulation in the reticuloendothelial system but also facilitates better surface modification, enhancing their biomedical utility [2] (Figure 3 and Figure 4).

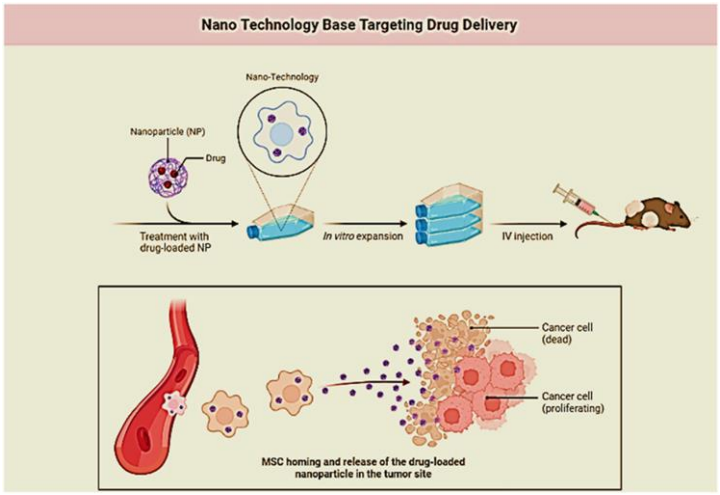

Fig 3. Steps of nanoparticle drug delivery system [9].

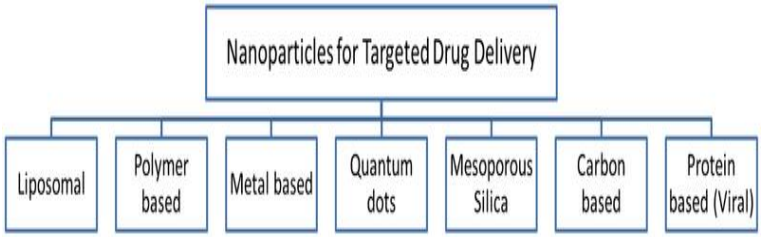

Fig 4. Different types of nanoparticle drug delivery systems [2].

2.4. Targeted biomarkers of nanoparticle drug delivery system

Different nanoparticle drug delivery systems have different targeted biomarkers, like Liposomal NPs have HER2 targeted biomarkers and polymer-based NPs have HER2 TNBC targeted biomarkers. Targe biomarkers have polymeric nanoparticles, liposomes, micelles, dendrimers, and inorganic nanoparticles. Polymeric nanoparticles are commonly used to encapsulate chemotherapeutic drugs, such as paclitaxel. Polymeric nanoparticles are used to improve their solubility and targeting. Liposomes can encapsulate drugs to improve stability and targeting and reduce side effects. Micelles are another form of nanoparticles that can co-deliver two or more drugs to enhance therapeutic effects. Dendrimers have a highly branched structure and can be used for targeted delivery of drugs. Inorganic nanoparticles have many different types such as mesoporous silica and gold nanoparticles. These particles can be used as drug carriers and for photothermal therapy.

2.5. Limitations of nanoparticle drug delivery system

Because of the benefits of using the nanoparticle drug delivery system, doctors use the nanoparticle drug delivery system more and more. Cancer bacteria also have evolution. That will cause the cancer bacteria to have resistance to the drugs. Like traditional drugs, these drugs also have lethal effects on people's bodies [10]. Since drugs are small using a nanoparticle drug delivery system, that makes the permeability of the drugs decrease. Drugs will accumulate around the vasculature and slow the release rate of drugs. To protect drugs from attracting normal tissues in the body, nanoparticle drugs have covers. Although this method protects drugs, it decreases the utilization factor of materials [11].

Liposome treatment is the most common treatment of nanoparticle drug delivery systems. It also has several disadvantages. Liposomes use targeted biomarkers to mark the positions of cancer bacteria due to the enhanced permeability and retention (EPR) mechanism. This method has not had high precision recently. Liposomes can reduce toxicity during treatment, but it does not mean that liposomes do not have toxicity at all. Liposomes produce some toxicity during the treatment [12].

3. Conclusion

There are many difficult diseases that doctors don't have good ways to cure. Cancer is the most common disease in people's lives. Breast cancer is the most common in women in the world. Many people died because of breast cancer. Traditional ways of breast cancer treatment are chemical treatment. Chemical treatments need patience and cost lots of time and money. These treatments also have serious side effects. To help patients cost less money and don't have so many side effects, scientists need to find better treatments to help people against breast cancer. Scientists find nanoparticle drug delivery systems are a good method. The nanoparticle drug delivery system has several benefits over traditional chemical treatments, like cheaper, less money, and more convenient and precise in curing breast cancer. Nanoparticle drug delivery system is abbreviated as NPs, and this system is based on liquid-based drugs. Like breast cancer, there are also several types of NPs. Different NP types have different routes of delivery and targeted biomarkers. However, everything has shortcomings, even the nanoparticle drug delivery system. Nanoparticle drugs can damage other tissues and organs, like traditional chemical treatment.

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