



Recent advances in nano-biotechnology for breast cancer therapy

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Abstract

One of the most common cancers in the world is breast cancer. The incidence of breast cancer has increased by more than 30% in the past 25 years, despite a significant decrease in fatality. On the other hand, due to the many advances in technology, even the best treatments for all types of cancer, including breast cancer, accessible today are not 100% efficacious. Therefore, many scientists are exploring new strategies based on nanotechnology to access more suitable options for breast cancer treatment and diagnosis. In recent years, to develop nanomaterials with unique properties many efforts have been made. Several of these attributes are used to expand tools to diagnose and treat cancers, including breast cancer. Nano-biotechnology and nano-drug delivery systems to cancer cells are a new method with the capability to enhance the immune system to identify and annihilate cancer cells with high selectivity. As a promising treatment, nano-medicines can not only eliminate primary tumors but are also effective in preventing metastasis and recurrence. Although much advance has been made, significant challenges yet need to be addressed. The purpose of this article is to review recent studies on the clinical therapy of breast cancer and provide new concepts about nano-drug transfer systems for anti-breast cancer drugs. Also, we review the main areas of nano-biotechnology research.

Keywords: Breast cancer, Nano-biotechnology, Nanoparticle, and Nano-drug delivery system

1 Introduction

Breast cancer is one of the most common cancers worldwide [1-3]. Breast cancer is the most common cancer in women and the second most common cause of death worldwide [4-6]. Despite a significant decrease in mortality, the incidence of breast cancer has increased by more than 30% in the last 25 years [7-10]. Breast cancer is a heterogeneous disease that exhibits different molecular profiles with distinct clinical and biological characteristics [11-13]. Breast cancer is the second most common cancer in women after skin cancer. Most breast cancers originate from the cells of the wall of the milk ducts and milk-producing lobules [14-16]. Breast cancer is a type of cancer that disrupts the function of cell division in breast cells. Breast cancer cells multiply uncontrollably and more than necessary in an infected person. There are different types of breast cancer, and their type depends on which type of breast cells are affected. Primarily, breast cancer is effected by virulent lesions in the breast conduit [17-19]. Every year, 500,000 mortality are caused by breast cancer in the world, and 1 out of every 10 women is diagnosed with breast cancer [20-23]. It should be noted, breast cancer is also common in men [14].

Studies have shown that if the mother has breast cancer, the chance of developing breast cancer in women doubles [24-26]. Also, women who don't breastfeed, late menopause and early menstruation, are more susceptible to breast cancer [27-30]. Factors such as obesity, drinking alcohol and smoking are associated with the development of breast cancer [31-34]. Therefore, the main factors in the occurrence of breast cancer can be mentioned as reproductive factors, genetic factors, environmental factors, and factors related to diet and lifestyle [14].

Breast cancer affects the life of sick's and their families and inflict a significant economic burden. As a result, improvement of primary diagnostic methods and new treatments are desperately necessary [35-37]. According to European guidelines, the diagnosis of breast cancer is based on clinical examination with imaging and is confirmed by pathological evaluation [38-40]. Although many advances have been made in cancer treatment and prevention, breast cancer treatment remains challenging. Breast cancer is mainly treated with surgery and chemotherapy [41-43]. Most patients prefer chemotherapy because surgery has a considerable psychological burden [14, 44-46]. Hence, chemotherapy drugs are usually very toxic, and conventional drugs cannot decrease their toxicity, consequently in intense side effects. Therefore, it is vital to choose effective drugs and appropriate treatment methods for breast cancer patients.

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Deracination of breast cancer and pursuant relapse can be provided by targeting breast cancer stem cells (BCSCs), yet clinical treatment is hampered by many factors, including the vague behavior of stem cells in breast tissue. Clinical treatment is only possible using multi-agent therapeutic profiles that simultaneously kill malignant cells along with BCSCs. Figure. 1. shows the effect of BCSCs on tumor progression and eradication [47-49].

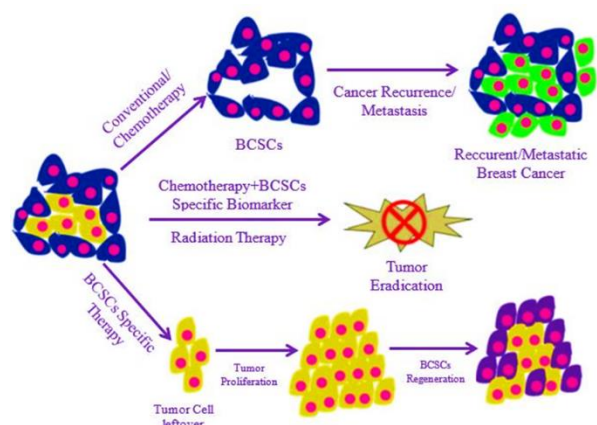


Figure 1. Effect of BCSCs on tumor progression and elimination [47].

2 Nano-biotechnology in cancer

Despite many technological advances, even the best treatments for all types of cancer, including breast cancer, are not 100% effective, and cancer still has a high mortality rate [4]. Although traditional breast cancer treatments are efficacious, they have several shortcomings, including considerable side effects [35, 50, 51]. Because of the side effects, such treatments reason inordinate harm to noncancerous cells. Therefore, in cancer treatment strategies there is an instant need to decrease cell toxicity [35]. On the other hand, the election of existing treatments pertains on tumor specifications such as biomarkers, tumor size, ligands, and metastatic sickness [52-54]. Therefore, many scientists are exploring new strategies based on nanotechnology to provide more options options for breast cancer treatment and diagnosis [55-58]. Nanotechnology is a new method that provide more effective the cure. This area of research has achieved promising results in clinical trials and has transpired as a treatment in the form of new drugs [4]. Nanotechnology offers unique features such as small (nanometer) size, active and passive targeting, binding to multiple targeting moieties, controlled release, and site-specific targeting [47]. Researches have shown, the transfer of chemotherapy drugs to tumor by nano-drug transfer systems can efficacious kill tumors, thus manufacturing it an efficacious strategy for treating diverse types of cancer, including breast cancer [14]. Nano-drug transfer are categorized into nanoparticles, liposomes, micelles and microemulsions based on their dispersion form, mode of motion, and physical structure, as shown in Figure 2 [14].

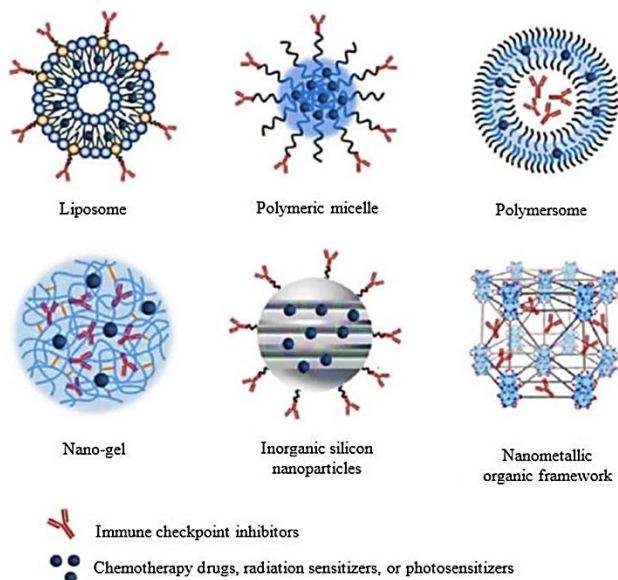


Figure 2. Schematic of the nano-drug transfer system [14].

Recent advances in technology and engineering have led to the application of nanotechnology in medicine with the development of new biomedical systems at the nanoscale. Nanomaterials have been investigated for biomedical research due to their extraordinary physicochemical properties. In particular, cancer nanotechnology has shown excellent approaches for cancer diagnosis and treatment with low toxicity compared to traditional cancer treatment [56]. In the case of drug delivery, nanomaterials can be designed to directly deliver chemotherapy drugs to cancer cells using specific antibodies to target the cancer site [59-61]. Therefore, both naturally derived nanoparticles and synthetic nanoparticles have been widely used in the treatment of various types of cancer due to their excellent compatibility and physicochemical properties [11]. It is well established that nanoparticles can be used for both diagnosis and transfer of therapeutic factors to tumors [62-64]. Therefore, considering all these reasons, new diagnosis strategies and effective treatments with less toxicity are urgently needed [65-67]. Nano-biotechnology, one of the essential fields, includes diagnosis and drug delivery in cancer [68-70]. Nano-biotechnology has the potential to improve early cancer detection and facilitate the personalization of cancer treatment. The most critical component of personalized medicine is a molecular diagnosis, and nano-biotechnology plays a vital role in its refinement and has led to the use of the term nano-diagnosis. Nano-biotechnologies also improve the detection of cancer biomarkers as a basis for devising diagnostics and treatments [71-74]. The most significant effect of nano-biotechnology is on the molecular diagnosis of cancer, which is also called nano-diagnosis. Nano-biotechnology is used to improve biomarker discovery, molecular diagnostics, drug discovery, and drug delivery, which are essential fundamental components of personalized medicine and can also be used for cancer management. The personalization of cancer treatments is based on a better understanding of the disease at the molecular level, and nanotechnology will play an essential role in this field. Nanotechnology is the creation and use of materials, devices, and

systems through the control of matter at the nanometer length scale, that is, at the level of atoms, molecules, and supramolecular structures. Nano-biotechnology is the application of nanotechnology in biological sciences, including molecular diagnosis, drug discovery, drug delivery, and nano-medicine development [68]. Nano-biotechnology is defined as the biomedical application of nano-sized systems. Nano-materials, that are a few nanometers in length, permit interaction with biological systems at the molecular surface. They can provide fundamental progress in the treatment and discernment of human cancers [75, 76]. Therefore, a better comprehension of biological processes and nano-biotechnology modifications will help improvement more suitable nano-medicine for breast cancer treatment in the future. Eventually, it is hoped that prevalent research will achieve the most by combining the described strategies so that the sick's tumor feature can be characterized in great detail [77-81].

3 Nano-biotechnology in breast cancer application

Nanotechnology is the creation and use of materials, devices, and systems through controlling matter at the nanometer scale. Different nanotechnologies and their applications in biological sciences are called nano-biotechnology [71, 82]. In recent years, plenty attempts have been made to develop nanomaterials. Some of these features are used to improvement tools to diagnose and treat breast cancer [35]. Also, diagnosis, treatment, and prevention may be possible thanks to the application of nanotechnology in clinical practice. Considering the different forms of breast cancer and disease status, nanomaterials can be designed to achieve the most important goals of modern treatment and diagnosis [56]. These treatments are targeted to increase efficacy and decrease toxicity. As a result, nanomaterials at the molecular surface enable proper interaction with biological systems, that has led to the improvement of "nano-biotechnology" applications in diagnostic imaging of tumors in vivo, tumor biomarker profiling, and providing targeted therapies [77]. Consequently, to dominate the restrictions of chemotherapy, nano-biotechnology provides a more targeted approach and thus can make it possible considerable benefits to cancer sick's. shape, charge, and size, are essential parameters in nanoparticle that show targeting ability, the uniform distribution, and biological destination [4]. Several nano-particle are they exist to target and transfer strong cancer medicines to damaged cells, so decreases toxic side effects. Research has developed so quickly that there are at present many breast cancer-special targeted drugs approved. These drugs target cancer cells, unlike non-targeted chemotherapy, which affects all cell. Side effects of targeted medicines are mild but sometimes severe [83, 84]. Nanoparticles can transport and release various types of factors to predetermined regions with great structural stableness (Figure. 3) [11]. Hence, there are numerous examples of work done using nanotechnology.

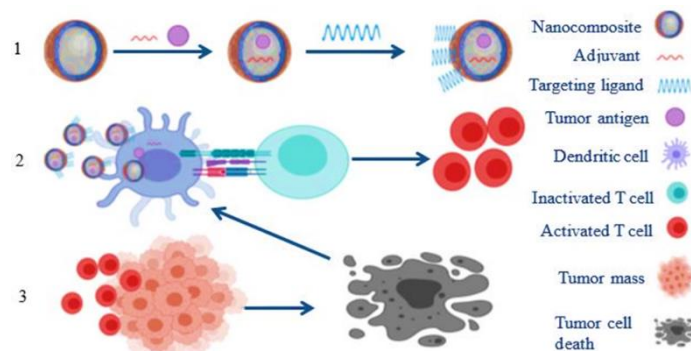


Figure3. The effect of nanoparticles in the activation of the body's immune system against cancer cells. 1. Addition of the target ligand on the surface of the nanoparticle. 2. Nanoparticle binding and T-cell activation. 3. response of T cells to cancer cells [11].

Bahreyni *et al.* [11] perused the performance of emerging nano-medicines for effective breast cancer immunotherapy. They concluded that as a promising remedy, immunotherapy could not only eliminate early tumors but is also effective in preventing metastasis and recurrence. Also, growing evidence suggests that nanotechnology may fulfill current cancer immunotherapy needs. White and co-workers, in a study, investigated nanotechnology approaches to deal with HER2-affirmative breast cancer [35]. They found that HER2-affirmative breast cancer usually spreads faster than other breast cancers. Therefore, targeted drugs are specially designed to prevent the growth of cancer. The results showed that nanotechnology could have significant effect in the identification, targeting, drug transfer, and demolition of tumors and cancer cells. Jaina and co-workers investigated nanotechnology-based approaches to breast cancer and triple-negative breast cancer [47]. They found that nanotechnology offers multiple approaches for imaging, monitoring, diagnosis, and delivery of chemotherapy medicines to the tumor site. Also, the results showed that nanoparticles help to deliver medicines with greater efficacy and reduced toxicity and can overcome biological barriers, thus improving anticancer activity. Nano-medicine is also a combination of material science, pharmacy, medicine, engineering, molecular biology, and information technology. They concluded that using nanoscience in medicine provides a way to study the biological system better and help understand the various mechanisms involved. In another work, Panariti *et al.* [85] reported the efficacy of nanoparticle absorption on cell demeanor. Their studies showed that although nanomaterials are beneficial in many vital applications, but tumors and cells do not answer to all types of nanoparticles similarly. Nanoparticle changes such as surface chemistry, shape, and size cause differences in the of cellular adsorption, responses, and their productivity in different biological applications. In another work, Cho *et al.* [86] reported a method to study the adsorption of gold nanoparticles with two disparate shapes. They showed that given the disparate shapes of nanorods and gold nanospheres, could be used to measure their concentrations in a instance. Most of the prevalent work is done in laboratory

conditions and on animals. Transferring these nano-designs from the laboratory to the infirmary is the next step to testing their safety and effectiveness on humans [35].

4 Advantages and disadvantages

In today's world, the use of nano-biotechnology and nano-carriers, despite all their advances in medicine, can bring the following advantages and disadvantages. Currently, there are several nano-medicines for the remedy of breast cancer. Nevertheless, most of these are being tested in clinical test [87]. Nano-drug transfer systems are mainly categorized into nanoparticles, liposomes, micelles, and microemulsions based on the dispersion form, mode of motion, and physical structure of nanoparticles [88-90]. These systems have become the focus of research in the ground of medicine transfer due to the benefits of improving medicine bioavailability and reducing medicine toxicity [91, 92]. Using nano-medicine transfer systems, medicines can be encapsulated and embedded within the nano-carriers or solubilized, adsorbed, and covalently attached to the surface of nano-carriers. It can not only increment the solvability of the drug and ameliorate its usage in biological systems but also take the drug to the target tumor site by using high retention effects and permeability in solid tumors and by manufacturing surface changes in the bearer. As a result, this helps increase the safety of the treatment and prevent the drug from being wasted by transferring it to normal tissues [93]. Targeting antitumor drugs through nano-carriers in anticancer therapy significantly reduces drug side effects and increases bioavailability [94]. Furthermore, since the tumor microenvironment influences drug liberation, drugs can be liberation sequentially or simultaneously. As a result, this reduces its toxicity and side effects on healthful tissues and improves the therapeutic effect of the drug.

It should be noted that drug transfer carriers have the following specification [95-98]:

- 1- They can penetrate the interstitial space, cross the blood-brain barrier, reside in specific tissue cells, and leisurely liberation the drug, thereby enabling targeted therapy.
- 2- They can improve bioavailability and the absorption rate of drugs, increase drug solubility, and optimize their pharmacokinetic properties.
- 3- Nano-drug transfer systems with a diameter of less than 200 nm can quickly passing through tissues. This decreases the risk of thrombosis when medicine-containing nanoparticles are injected.
- 4- They have also been successfully used in treatment and medical diagnosis due to the advantages of reduced medicine toxicity, precise targeting, and medicine availability [99].

Studies have shown that transfer of chemotherapy medicines to tumor sites using nano-medicine transfer systems can effectively kill tumors, thus making it an efficient strategy for breast cancer treatment [14]. To make a suitable nano-carrier for fast and effective clinical diagnosis, some essential features should be considered. Nano-carriers should be built of a material that is easily usable and biocompatible, soluble, and able to show more extended blood circulation, non-aggregation, and high adsorption yield by target cells. As mentioned, nano-carriers can be categorized into three categories based on the materials they are made of 1- inorganic, 2- lipid-based, and 3- polymeric. These

nano-carriers are used for various applications such as imaging, diagnosis, drug delivery, treatment, and etc.

One of the determining factors of drug dispensation in tissues is the half-lifetime of circulating drugs. A drug with a more half-lifetime will have a more uniform dispensation in the tissues, even if its excretion and influence into the tissues are relatively sluggish. In contrast, a drug with a stunted moiety-life will have a non-uniform distribution [100]. Studies show that the quantity of drug piled up naturally is 10 to 20 times greater than a tumor site of the same weight, and many anticancer drugs cannot penetrate more than 40 to 50 mm [101-104]. These defects mostly lead to multiple drug resistance (MDR), incomplete tumor response, and ultimately, treatment failure [105-107]. When the tumor are treated with an anti-cancer drug, they become resisting to the full spectrum of drugs. Generally, MDR occurs based on the excessive secretion of the drug, and Hence, it is a fundamental challenge for breast cancer treatment [108-111].

5 Conclusion and futures outlooks

Breast cancer affects the of life of sick's and their families. As a result, improvement of primary methods and new treatments are severely needed. Although many advances have been made in cancer treatment and prevention, breast cancer treatment remains challenging. Nanotechnology is a new method that provide more effective treatment. This sphere of research has emerged in the form of new drugs and has achieved promising results in clinical tests. These treatments are targeted to increase efficacy and decrease toxicity. As a result, nanomaterials at the molecular surface enable proper interaction with biological systems, that has led to the improvement of "nano-biotechnology" applications in diagnostic imaging of tumors in vivo, tumor biomarker profiling, and providing targeted therapies. Consequently, to prevail the restrictions of chemotherapy, nano-biotechnology offers a more targeted approach and can provide considerable benefits to cancer sick's. Therefore, understanding of biological processes and nano-biotechnology modifications will help develop more compatible nano-medicine for breast cancer treatment in the future. Eventually, it is hoped that prevalent research will achieve the most by combining the described strategies so that the sick's tumor feature can be characterized in great detail.

Ethical issue

Authors are aware of, and comply with, best practice in publication ethics specifically with regard to authorship (avoidance of guest authorship), dual submission, manipulation of figures, competing interests and compliance with policies on research ethics. Authors adheres to publication requirements that submitted work is original and has not been published elsewhere in any language.

Competing interests

The authors declares that there are no conflict of interest that would prejudice the impartiality of this scientific work.

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