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Nanoparticles in Breast Cancer Management

Muhammad Imran Qadir and Maryam Zahra

ABSTRACT

Nanotechnology deals with the study of extremely small things of nanosize, and it plays a significant role in industrial, agricultural, and medicinal fields. Various nanoparticles/nano-techniques have been developed, which play a key role in cancer medicine, especially for breast cancer treatment and diagnosis. Breast cancer is the second most common cause of death from cancer in women in the United States after lung cancer. Nanoparticles, in combination with other therapeutic approaches to breast cancer treatment, give exceptional results to patients in their recovery from this life-threatening disease. Applications of different nanoparticles in breast cancer management include viral nanoparticles, reduction in breast cancer cell metastasis via RNA-based TWIST1 inhibition using the dendrimer complex, encapsulated nanoparticles with neuropeptide Y Y1 receptors support targeted anticancer drugs delivery to breast cancer cells, using curcumin-encapsulated nanoparticles for antiproliferation of aggressive breast cancer cells, enhancing chemotherapy in inflammatory breast cancer cells through nanoshell-mediated photothermal therapy, poly(butylcyanoacrylate) nanoparticles and antitumor activity of doxorubicin in breast cancer therapy, nanoparticle albumin-bound paclitaxel and managing some dangerous events in patients with breast cancer, antiproliferative effect of anti-miR-21- and 4-hydroxytamoxifen-co-loaded biodegradable nanoparticles on breast cancer cells, breast cancer therapy using 5-fluorouracil-loaded methoxy-poly(ethylene glycol) poly(lactide) nanoparticles, nanoparticles for co-delivery of an anticancer drug and siRNA for triple-negative breast cancer cells, chitosan-layered gold nanorods for gene silencing in triple-negative breast cancer. Many other nanoparticles have also been discovered for breast cancer management that have made breast cancer therapy more advanced and quicker.

Keywords: Nanoparticles, Breast cancer therapy, Dendrimer complex, TWIST1 inhibition, Curcumin-encapsulated nanoparticles

Introduction

Nanotechnology is the study of very tiny structures (1–1,000 nm). Precisely, when individual atoms, compounds, or molecules of this size are converted to produce devices, structures, or materials with special properties, the branch of science is known as nanotechnology.¹ Nanotechnology plays an extremely important part in the advancement of medical science and drug delivery.² Apart from medicine, nanotechnology is also important for industrial applications. For instance, at present, nanotechnology is developed as a potential tool to increase global production of various agricultural products because the demand for nano-fertilizers

is increasing rapidly among populations. These nano-fertilizers can increase the yield of crops or combat harsh environments and plant-growth-enhancing nanomaterials, which can increase, among other things, the agronomic yield of crops.^{3,4} Nanotechnology offers unusual breakthroughs in the treatment of diseases by providing different opportunities for developing vaccines, novel treatment methods, diagnostic tools, gene therapy, and a direction toward personalized medicines.⁵ Nanomaterials are those that measure 1–1,000 nm and allow for a unique relationship with biologics at the level of molecules. Nanoparticles are developed for the imaging of tumors in vivo and also for bio-molecular profiling of cancer biomarkers and delivery of many other drugs. Nanomaterials that are useful in medicine are referred to as nanomedicine, and the objective of nanomedicine is to raise the therapeutic uses of medicinal things with a reduction in the toxic effects and increase the drug's therapeutic index.⁶ The functioning of nanoparticles with tumor-specific proteins or cytotoxic drugs has proven a very promising technique in cancer research to target tumor cells, improve drug delivery, and decrease systemic toxicity of drugs.^{7,8} Surface-engineered nanocarriers, which have many different strategies like ligand, glycosylation, antibody conjugation, PEGylation, and acetylation have been discovered for treating various disorders such as cancer; HIV/AIDS; neurodegenerative, autoimmune, and genetic diseases; and development of artificial organs.² The rate of success of nanotechnology in medicine is evinced by the presence of marketed formulations based on nanomaterials.^{9,10}

In the United States, breast cancer is the main reason for cancer-related deaths among women, with over 235,000 new diagnoses and approximately 40,000 deaths in 2014. This is the second leading reason for deaths among females worldwide, and more deaths are reported in developed countries.¹¹ Nonmetastatic breast cancer can be well-managed with chemotherapy, radiation, and surgery. Metastatic breast cancer (MBC) spreads to the brain, liver, bone, and lungs, and it is frequently not curable. Triple-negative breast cancer (ER-negative, HER2-negative, and progesterone-receptor-negative) is of special interest, as it is very aggressive and metastatic and does not respond to current and recent therapies.¹² Breast cancer is a life-threatening cancer, and it is the most common malignancy with high incidence rates among women in the whole world. Despite advancements in chemotherapeutic treatment, the most prominent metastatic property of breast cancer cells is still a challenge to the available therapeutic regimens. Currently, different nanoparticles are being discovered for the treatment and diagnosis of breast cancer.^{13,14}

The history of breast cancer dates back to around 1500 BC. The ancient Egyptians reported this disease

more than 3,500 years ago for the first time. Breast cancer is similar in males and females. Breast cancer in males is more frequently hormone-receptor-positive and might be much more sensitive to hormonal therapy. Tumors of the male breast are more likely to express the estrogen and progesterone receptors and less likely to overexpress HER2 than breast cancer in women. Presentation is mostly a lump or nipple inversion. It is often diagnosed late, with more than 40% of individuals diagnosed at the third or fourth stage of the disease.¹⁵ Therefore, different nanomaterials or nanoparticles are developed to treat breast cancer efficiently, for example, silver nanoparticles (Figure 1). These nanoparticles, in combination with other therapeutic approaches to breast cancer treatment, give exceptional results on patients to recover from this dangerous disease. Different studies related to the use of nanoparticles for breast cancer management were selected by reviewing the literature on different sources of information, including Google Scholar, ScienceDirect, and PubMed

A Comparative Analysis of the Different Nanoparticle Types

Green synthesis, chemical, physical, biological, coprecipitation, hydrothermal treatment, flame pyrolysis, biogenic reduction, and microbial processes are the different methods by which different types of nanoparticles may be synthesized. Many hazardous effects have been reported due to chemical synthesis, so the potential utility of nanomaterials is also recognized in environmental management, as there is growing demand to control diverse pollutants. At present, there is a green synthetic route for the development of nontoxic and eco-friendly materials in a sustainable manner.¹⁶

Different nanoparticles are used for breast cancer treatment. Some of the therapeutic uses of important nanoparticles for the treatment of breast cancer are discussed below.

Viral Nanoparticles

When a virus is emptied from its genetic material, drugs can be loaded into the empty virus capsid. This

carrier system is advantageous for its nanostructure and capsid surface. The capsid surface of this carrier is biologically active.¹⁷ A significant viral carrier system was invented in conjugation with a cytotoxic agent or radiation. It was invented in a registered patent by the University of Sydney. This system is a genetic modification to increase the expression of insulin-like growth factor binding protein-5 by the cell to an amount that induces apoptosis. Cowpea chlorotic mottle virus, bacteriophages, cowpea mosaic virus, and canine parvovirus are viral nanoparticles that are being used.¹⁵

RNA-Based TWIST1 Inhibition Using Dendrimer Complex

Twist-related protein 1 (TWIST1), also known as class A basic helix-loop-helix protein 38 (bHLHa38), is a basic helix-loop-helix transcription factor that in humans is encoded by the TWIST1 gene. This gene encodes a basic helix-loop-helix (bHLH) transcription factor that plays an important role in embryonic development. Nanotechnology is helpful in the reduction of breast cancer cell metastasis via RNA-based TWIST1 inhibition using the dendrimer complex. It is critical to understanding the mechanism of cancer metastasis so as to identify novel therapeutic targets and discover new therapies for better outcomes for patients. A transcription factor, TWIST1, is overexpressed in aggressive breast cancer. It is the main regulatory factor of cellular migration by epithelial-mesenchymal transition (EMT).

A siRNA-based TWIST1 silencing approach with a delivery system using a modified poly(amidoamine) (PAMAM) dendrimer is demonstrated in this study.¹⁸ SUM1315 TNBC cells take up PAMAM-siRNA complexes efficiently. This leads to the knockdown of TWIST1- and EMT-related target genes. After transfection, knockdown lasts for up to one week. This leads to a decrease in migration or invasion, which is determined through transwell assays and wound healing. Then, PAMAM dendrimers are demonstrated, which can transfer siRNA to patients' orthotopic tumors. At least for four hours after treatment, siRNA remains in the tumor. The results further suggest that more development in dendrimer-based delivery of siRNA for silencing TWIST1 could give beneficial adjunctive therapies for patients having triple-negative breast cancer.¹²

These data also support investigations in using siRNA with nanoparticles for the treatment of malignant breast cancer. This can be done by knocking down TWIST1 and its related epithelial-mesenchymal transition targets. Furthermore, these data provide evidence that TWIST1 is a clinically powerful therapeutic target for treating metastatic breast cancer and solid tumor cancers.¹⁹

Encapsulated Nanoparticles with Neuropeptide YY1 Receptors

Encapsulated nanoparticles with neuropeptide Y Y1 receptors support targeted delivery of anticancer drugs to breast cancer cells. Neuropeptide Y receptors are highly overexpressed in breast tumors of human beings. Expressed subtypes between tumor breast tissues

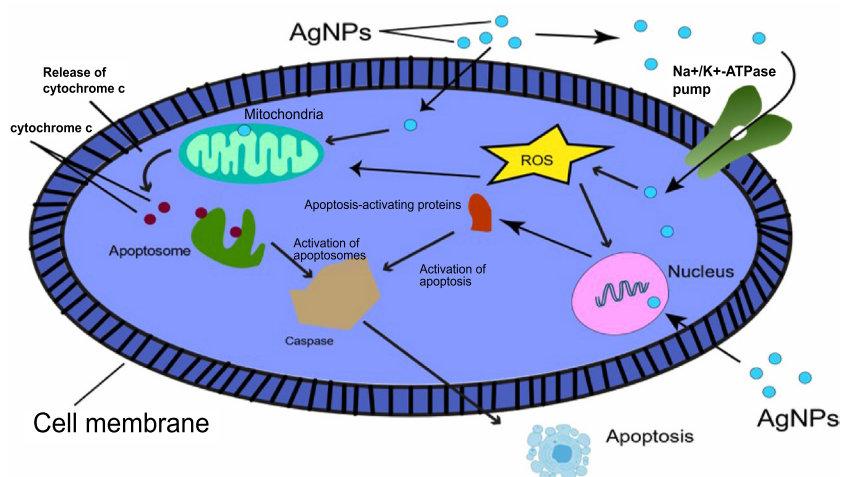


Fig 1 | Silver nanoparticles in breast cancer management

and normal breast tissues are markedly different.²⁰ A selective Y1Rs ligand [Pro, Nle, Bpa, Leu] NPY (28–36) with the anticancer drug doxorubicin (DOX)-loaded albumin nanoparticles (ANP) is used in this study. It is usually abbreviated as PNBL-NPY-DOX-ANP. It is used to observe the effects of Y1Rs on the delivery of some anticancer-drug-encapsulated nanoparticles to human breast cancer cells and used for its role in breast cancer treatment.²¹

The use of Y1Rs ligand PNBL-NPY, a targeted molecule used to deliver some DOX-encapsulated biocompatible albumin nanoparticles to breast cancer cells and its important role for breast cancer therapy, is demonstrated here. It is revealed that PNBL-NPY can recognize Y1Rs and bind to Y1Rs.²²

This is a highly selective system, and it is able to differentiate breast cancer cells from some normal cells because only Y2Rs are expressed in normal breast cells. Furthermore, the efficient targeting ability of PNBL-NPY-DOX-ANP plays an important part in improving breast cancer therapy. This is due to the following advantages: (1) improvement in the delivery of DOX-ANP can transfer more doxorubicin into the breast cancer cells, and inducing a strong inhibitory effect on the growth of the cells; and (2) PNBL-NPY ligand could cause a symbiotic effect to inhibit breast cancer cell growth. PNBL-NPY could be utilized as an innovative active target molecule that can deal with delivering of drug-encapsulated nanoparticles in the breast cancer cells with great selectivity and less harm to normal breast cells.

Guidance is provided by this study to make some new Y1Rs-based nanoparticle drug delivery systems for safe and efficient breast cancer treatment.²³

Curcumin-Encapsulated Nanoparticles

The main objective of this study is to evaluate the effect of delivery of anticancer drugs such as curcumin for safe and affordable cancer therapy using nanotechnology and electrical pulses. Curcumin is a natural herbal extract of turmeric. It is also known for its anti-inflammatory, antioxidant, and antitumor properties.²⁴ It inhibits expression of these signals: (1) proliferating cell nuclear antigen (PCNA); (2) Ki-67; (3) p53 mRNAs in breast cancer cells; and (4) induced mRNA expression by downregulation of p21 mRNA in the human mammary epithelial cells.²⁵ The use of curcumin is, however, limited because of its short biological half-life (13 ± 3.5 hours). A dual technology is implemented to increase this nontoxic absorption of curcumin in tumor tissue: (1) curcumin was encapsulated in the nanoparticles (CNP) to enhance its availability; and (2) applying low electroporation (EP).

CNP was tested (in vitro) on breast cancer cells of MDA-MB-231, (ATCC HTB-26) to evaluate this study.²⁶ Two groups (untreated control and CNP + EP treated) in triplicate were tested. Breast cancer cells (1×10^6 cells) of >98% viability in 1% PBSA were treated with CNP (0, 200, 400, and 600 μg equivalent of curcumin) in each well. Electrical pulses were administered for six, 1,200V/cm, 100 μs to deliver CNP into the cells after

treatment and to study their antitumor activity over a period of 72 hours by counting dead and live cells. Results of this study showed that the effect of combined treatment of CNP+EP provides a new alternative to increase the efficiency of cancer treatment.^{27,28}

Nanoshell-Mediated Photothermal Therapy (PTT)

PTT refers to efforts to the use of electromagnetic radiation for the treatment of various medical conditions. Enhancing chemotherapy in inflammatory human breast cancer cells through nanoshell-mediated PTT is also an important therapy that uses nanoparticles for breast cancer patients. A standalone therapy for the treatment of cancer is nanoshell-mediated photothermal therapy.²⁹ Loss of membrane integrity is a cellular effect of PTT. Scientists presented a hypothesis that by improving the accumulation of drugs in cancer cells, nanoshell-mediated photothermal therapy can have a potential effect on the cytotoxicity of chemotherapy.³⁰ Here, this hypothesis is verified using doxorubicin, which is used as a model drug. A model cancer subtype, SUM149 inflammatory breast cancer cells, was used. The SUM149 cells were initially exposed to nanoshells. Then, they were exposed to near-infrared light, and after that, SUM149 cells were stained with ethidium homodimer-1. Ethidium homodimer-1 is extracted from cells with intact plasma membranes. Results showed that nanoshell-mediated photothermal therapy could enhance the permeability of the membrane in SUM149 cells.^{31,32} In corresponding experiments, SUM149 cells that were treated with nanoshells, near-infrared light, or a combination of both were exposed to fluorescent rhodamine 123.

Analyzing rhodamine 123 fluorescence in the cells confirmed that PTT causes an increase in membrane permeability and could increase the accumulation of the drug in cells. The intracellular distribution of doxorubicin was assessed using fluorescence microscopy. In other experiments, to determine whether the uptake of drugs by PTT is enough to increase cell death, SUM149 cells were exposed to subtherapeutic levels of doxorubicin, low-dose PTT, or a combination of two treatments. An analysis of the experiments revealed a minimum loss of viability relative to controls in the cells that were exposed to subtherapeutic amounts of doxorubicin, about 35% loss of viability in the cells that were exposed to combined therapy, and about 15% loss of viability in cells exposed to the low-dose photothermal therapy. The data also shows that nanoshell-mediated PTT warrants further investigation using other drugs and cancer subtypes.³³

Poly(butylcyanoacrylate) Nanoparticles and Doxorubicin Antitumor Action

One of the most efficient molecules in treating metastatic breast cancer is doxorubicin (DOX). Its use is limited as it has minimal tumor selectivity and harmful side effects. Poly(butylcyanoacrylate) nanoparticles (PBCA NPs) may increase the antitumor activity of doxorubicin against breast cancer cells. This allows a decrease in the effective dose required for antitumor

activity and, as a result, the level of relative toxicity. DOX loading on poly(butylcyanoacrylate) nanoparticles was investigated through drug entrapment and surface adsorption. Using human breast tumor cells (MCF-7), cytotoxicity assays with efficient DOX-loaded nanoparticles were performed in *in vitro* experiments.

More values of drugs' loading and controlled profile of drug release were produced by the entrapment method. The 50% inhibitory concentration of doxorubicin-loaded poly(butylcyanoacrylate) nanoparticles was lower for many MCF-7 and E0771 cancer cells as compared with free doxorubicin. Doxorubicin-loaded poly(butylcyanoacrylate) nanoparticles produced growth inhibition in the tumor. It was greater than 40% than that observed with free doxorubicin, thus decreasing the toxicity of doxorubicin during treatment. The results verify that poly(butylcyanoacrylate) NPs may be utilized to increase the efficacy of doxorubicin therapy against breast cancers. The improved antitumor activity of doxorubicin-loaded poly(butylcyanoacrylate) nanoparticles might be used to decrease the DOX dose that was important for an adequate antitumor effect having negligible toxicity.³⁴

Ceria Nanoparticles

One of the main strategies for the treatment of cancer is radiotherapy. It has some challenges, like cancer cell resistance and disruption of normal tissues by radiation. The susceptibility of cancer cells to radiation is increased by radiosensitizers. These increase the effect of radiotherapy. The development of a new radiosensitizer that consists of monodispersed ceria nanoparticles (CNPs) with an anticancer drug neogambogic acid (NGA-CNPs) is reported in this study. The efficacy and mechanisms of action of this treatment approach were evaluated in conjunction with radiation in MCF-7 breast cancer cells. Neogambogic acid CNPs enhance the toxicity of radiation. This leads to a higher cell death rate than the treatment used alone. It induces activation of autophagy, and then the cell cycle is arrested at the G2/M stage. Pretreatment with neogambogic acid or CNPs has not improved the rate of death of cancer cells induced by radiation. NGA-CNPs, unlike some other nanomaterials, reduced the formation of endogenous and radiation-induced active oxygen species. These results provide information that the combined use of NGA-CNPs can raise the efficacy of radiotherapy in the treatment of breast cancer. This can be done by decreasing the doses of radiation used to kill the cancer cells, hence minimizing damage to adjacent healthy tissue.³⁵

Nanoparticle Albumin-Bound Paclitaxel

Paclitaxel and docetaxel are included in taxanes. Both taxanes and anthracyclines are essential agents in chemotherapy for the treatment of breast cancer. Due to the better efficacy and tolerability of paclitaxel, weekly paclitaxel has been widely used in Japan.³⁶ The effectiveness of nab-paclitaxel therapy was analyzed retrospectively in this study. This analysis was done on 22 patients with metastatic breast cancer. These patients were treated

between November 2010 and June 2012 at the National Hospital Organization Shikoku Cancer Center. The median age of patients was about 59 years. Nab-paclitaxel was administered in patients once every three weeks. In 63.6% of patients, the tumors were progesterone- and/or estrogen-receptor-positive. The median of the treatment cycle was six. No patients with breast cancer were HER2-positive. In six patients, the rate of response was 27.3% and the rate of clinical benefit was 31.8%. In those patients who received nab-paclitaxel as the first- or second-line treatment, the rate of response and rate of clinical benefit were higher. During treatment, peripheral neuropathy (59%), myalgia (59%), vomiting (50%), and rash (45%) were the adverse events. Hence, this study suggests that nab-paclitaxel is a clinically beneficial anticancer preparation.³⁷

Anti-miR-21- and 4-Hydroxytamoxifen-Coloaded Biodegradable Nanoparticles

The second major reason for cancer-related deaths in women is breast cancer.³⁸ A broadly employed antiestrogen is tamoxifen. Tamoxifen is used as a treatment option for early and more advanced estrogen-receptor-positive breast cancers in women and as the most common hormonal therapy for breast cancer in males. Most breast tumors are hormone-dependent and estrogen-receptor-positive (ER+). To decrease tumor mass before surgery, neoadjuvant antiestrogen treatment has been widely used.³⁹

An active metabolite of tamoxifen is 4-hydroxytamoxifen (4-OHT). It functions as a receptor antagonist of estrogen and displays a strong affinity for estrogen receptors.⁴⁰ A noncoding RNA of 23 nucleotides is MicroRNA-21 (miR-21). It regulates many apoptotic and tumor suppressor genes. miR-21 contributes to the chemoresistance in several cancers.^{41,42}

The therapeutic role of 4-hydroxytamoxifen and anti-miR-21 coadministration in an attempt to compete against tamoxifen resistance is investigated in this study. Tamoxifen resistance is a common problem that is being encountered by antiestrogen therapy.

4-OHT- and anti-miR-21-coloaded PLGA-b-PEG NPs were discovered by using the following methods: (1) emulsion-diffusion evaporation; and (2) water-in-oil-in-water double emulsion.

A biodegradable copolymer, poly(D,L-lactide-co-glycolide)-block-poly(ethylene glycol) (PLGA-b-PEG-COOH), was used as a carrier for co-delivering 4-OHT and anti-miR-21 to estrogen-receptor-positive breast cancer cells. Optimal NPs were prepared using the double emulsion method. These nanoparticles were evaluated according to their apoptotic and antiproliferative effects against various human breast cancer cells (MCF-7, ZR-75-1, and BT-474). The best method for 4-OHT loading was emulsion-diffusion evaporation method. The water-in-oil-in-water procedure was the best for co-loading nanoparticles with 4-OHT and anti-miR-21. A treatment of MCF-7 cells with 4-OHT- and anti-miR-21-coloaded different NPs is indicated by MTT assays. The result of this treatment is dose-dependent antiproliferative effects at 24 hours.

This effect was higher than that achieved with 4-OHT at 48 hours and 72 hours posttreatment.

It was suggested by analysis of cell proliferation that 4-OHT- and anti-miR-21-co-loaded nanoparticles significantly inhibit MCF-7 cell growth as compared to free 4-OHT and untreated cells at 1 μ M concentration.⁴³ There was no proper difference in the growth rate of MCF-7 cells treated with control nanoparticles or nanoparticles loaded with anti-miR-21 and the growth rate of untreated MCF-7 cells. The use of the PLGA-b-PEG polymer nanoparticles as an efficient nanocarrier for codelivery of anti-miR-21 and 4-OHT, and the role of this drug combination in treating estrogen-receptor-positive breast cancer are demonstrated from these findings.⁴⁴

5-Fluorouracil-Loaded Methoxy Poly(Ethylene Glycol)-Poly(Lactide) Nanoparticles

Worldwide, 23% of total cancer cases with 15% of cancer-related deaths among females are due to breast cancer, making it one of the deadliest diseases.⁴⁵

A new nanocarrier was discovered for delivering an anticancer drug to breast cancer tissues in this study. 5-Fluorouracil-loaded methoxy poly(ethylene glycol)-poly(lactide) (mPEG-PLA) (5-FUNP)-based polymeric nanoparticles were being developed for this purpose. These nanoparticles increase the efficacy of chemotherapy against breast cancer.⁴⁶

Drug-loaded nanoparticles were synthesized using the nanoprecipitation method. The average particle diameter of drug-loaded nanoparticle was approximately 110 nm. It showed a sustained drug release pattern for 120 hours. The increased cytotoxicity effect of nanoparticle formulations compared to free drug in vitro was shown by cytotoxicity assay. The nanoparticle system presented good G2/M phase of the cell cycle arrested with some significant levels of apoptosis in late- and early-phase analysis by flow cytometer analysis.

Nanoparticle formulation reduced some tumor burdens in patients with no lethal effects. TUNEL assay confirmed the better anticancer effect of nanoparticle formulations that showed a good number of apoptotic cells. The application of encapsulated 5-fluorouracil nanoparticles in treating breast cancers provided the results obtained from this study.⁴⁷

Layer-by-Layer Nanoparticles

Triple-negative breast cancer is a subtype of breast cancer. It is linked with poor prognosis, and it has no good standard-of-care therapy.⁴⁸ Layer-by-layer NPs use the process of sequential depositing of oppositely charged polymers to make a stable film with a high siRNA content top. A nano-sized core provides an exceptional new class of drug delivery platform with a better clinically translational potential.⁴⁹

Through a controlled layer-by-layer process for codelivering siRNA, a single nanoparticle platform has been efficiently developed. It knocks down a chemotherapeutic drug to challenge aggressive form of triple-negative breast cancer and also a drug resistance pathway in tumor cells. By alternately depositing

siRNA and poly-L-arginine, layer-by-layer films were formed on nanoparticles. It is a single bilayer on the surface of a nanoparticle that can load effectively up to 3,500 siRNA molecules. Hence, the resulting layer-by-layer nanoparticles have an increased half-life of the serum of about 28 hours. In animals, one dose through intravenous administration decreases the target expression of genes by almost 80% in tumors. A doxorubicin-loaded liposome, a good combined therapy with targeting of siRNA multidrug resistance protein 1, was identified by developing an siRNA-loaded film top. This significantly increases the efficacy of doxorubicin in vitro by 4-fold. Then, it leads to 8-fold decrease in the volume of the tumor as compared to the control treatments with less or no toxicity.⁵⁰

It is indicated by these results that using layer-by-layer films to change a liposomal doxorubicin delivery system with a siRNA leads to a decrease in tumors in those cancers that are nonresponsive to treatment only with Doxil. This approach is a good treatment for aggressive cancers.

Chitosan-Layered Gold Nanorods

Chitosan-layered gold nanorods are studied for silencing genes in triple-negative breast cancer. Recent studies show that metallic nanoparticles are useful for nanomedicine applications because of their optical and electrical properties.⁵¹ Gold nanoparticles indicate better promise due to biocompatibility, photothermal responsiveness, and effortlessness in preparation and modification. In particular, gold nanorods (AuNRs) have been extensively used for biomedical applications, including photothermal therapy, drug delivery, and biosensing.⁵²

Small interfering RNAs (siRNAs) are widely studied due to their great potential as therapeutic agents for a variety of diseases, including cancer. The efficient delivery of siRNAs to target cells and tissues remains challenging due to the lack of suitable delivery systems. A layer-by-layer assembled chitosan-gold nanorods (Chit-Au NRs) siRNA delivery system is studied here to overcome the biological barriers to systemic injection. This platform can protect siRNAs from degradation upon exposure to ribonuclease or serum. Confocal and intravital microscopy shows that Chit-Au NRs / siRNAs are delivered successfully into target cells and tissue. They can also escape from endosomal/lysosomal structure efficiently. In tumor tissue, Chit-Au NRs / siRNA accumulate in large amounts.

The oncogene expression (pyruvate kinase isozyme M2, PKM2) in MDA-MB-231 of triple-negative breast cancer cells was inhibited by this delivery system. This results in suppression of the proliferation and migration of cells. Furthermore, the anticancer efficiency was increased by NR-mediated photothermal ablation. In conclusion, the therapeutic properties of Chit-Au NRs / siRNA cause suppression of cancer growth.⁵³

Targeting cancer cells and avoiding noncancerous cells is the holy grail of therapy for cancer. Many different systems and strategies have been designed for targeting tumors over the years. Over the course of the

Table 1 | Various types of nanoparticles for treatment of breast cancer

Various Nanoparticles for Treatment of Breast Cancer	References
Stealth doxorubicin-loaded magnetic nanovectors on breast cancer patients	54
Nanoparticles with hydrogel doping for release of siRNA in breast cancer	55
Folate decorated nanoparticles for MR imaging and targeting of human breast cancer cells	56
AS1411-conjugated gold nanospheres for breast cancer therapy	57
Silver nanoparticles and their therapeutic applications in breast cancer	58
Gold nanoparticles in the diagnosis and treatment of breast cancer	59
Poly(ethylene glycol)-block-poly(ϵ -caprolactone) and phospholipid-based nanoparticles for breast cancer therapy	60
Docetaxel-loaded solid lipid nanoparticles for the treatment of cancer	61
Photoimmunotherapy for breast cancer by poloxamer blend nanoparticles	62
Cationic polymer-modified mesoporous silica nanoparticles	63
Targeting of a gold nanoparticle for breast cancer metastasis	64
Treatment of breast cancer through iron oxide nanoparticles	65
A nanoparticle, manumycin, for cell death in triple-negative breast cancer	66
Docetaxel and poloxamer 235 by PLGA-TPGS nanoparticles in breast cancer treatment	67
Rapamycin- and piperine-loaded polymeric nanoparticles for breast cancer treatment	68
Nanoscale β -1,3-glucan improves HER2-positive breast cancer therapy	69
Magnetic nanoparticles heating in breast cancer treatment	70
Manganese-oxide- and docetaxel-coated fluorescent polymer nanoparticles for chemotherapy of breast cancer	71
Chitosan nanoparticles in breast cancer cells	72
Silver nanoparticles	73

past decade, many different acquisitions have been made in the pharmaceutical industry in this critical field of research. For these reasons, emerging pharmaceutical and nanotechnology companies try to increase their patent portfolio to increase their commercial value for possible buyouts by big pharmaceutical firms.⁷⁴ Currently, many patents focus on bioconjugate structures, which are manufactured easily with very high-yield, minimum-cost, and high-stability profile of the final formulation.¹⁵ It is concluded from the above literature that different nanoparticles such as viral nanoparticles, gold nanoparticles, silver nanoparticles, ceria nanoparticles, doxorubicin-loaded nanoparticles, curcumin-encapsulated nanoparticles, and 5-fluorouracil-loaded methoxy poly(ethylene glycol)-poly(lactide) nanoparticles are being used for therapy of different forms of breast cancer. Many other latest nanoparticles for breast cancer therapies are listed in Table 1.

Current Gaps in the Literature

Current gaps in the literature related to nanotechnology and breast cancer primarily stem from an insufficient understanding of the long-term safety, toxicity, and biodistribution of nanoparticles in vivo. Moreover, there is a lack of advanced, noninvasive imaging techniques to track nanoparticles in real time, and targeting specific tumor microenvironments with high precision is still an unresolved issue. These gaps in the literature related to nanotechnology and breast cancer hinder the widespread clinical application of nanotechnology in breast cancer management.

Potential Challenges

The science of nanomedicine holds substantial possibilities for evolving breast cancer management, but numerous challenges persist that hinder its common

clinical use in practice. The safety and long-term toxicity of nanoparticles in humans remain underexplored, particularly regarding their accumulation in nontarget tissues and potential immunological reactions. Another issue is the difficulty in achieving uniform drug release from nanoparticles, which can affect therapeutic efficacy.

Conclusion

Nanotechnology could provide a practical direction for the development of novel management tools and therapeutics for breast cancer for researchers worldwide, paving the road to affordable, scalable, stable, efficient, and safe management strategies.

Future Directions

The future of nanotechnology in breast cancer treatment holds great promise, particularly in enhancing early detection, targeted drug delivery, and personalized therapies. Advances in nanomaterials, such as nanoparticles, quantum dots, and nanosensors, are expected to enable more accurate and noninvasive detection of tumors at the molecular level, even before they become visible through traditional imaging methods.

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