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NANOPARTICLES IN BREAST CANCER THERAPY: A COMPREHENSIVE REVIEW

M. Sai Akash, G. Tulasi Saranya, B. Meghana, L. B. S. Sasidhar, K. Deepthisree, M. Dyva Krupa and V. Rama Rao*

Department of Pharmaceutics, Shri Vishnu College of Pharmacy, Vishnupur, Bhimavaram, West Godavari, A.P, India-534 202.

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***Corresponding Author**
Dr. V. Rama Rao
Department of Pharmaceutics, Shri Vishnu College of Pharmacy, Vishnupur, Bhimavaram, West Godavari, A.P, India-534 202.

ABSTRACT

Breast cancer (BC) is one of the most Common diagnosedcancers in women, which ranks the second leading cause of cancer deaths in women across the world. Now a day's most of the anti-cancer medications develops high potential toxicity and carcinogenic effects in patients. Hence Nanoparticles are identified for their effective treatment against breast cancer, which are known for their enhanced safety and efficacy. Nanoparticles are the target drug delivery systems which may improve the pharmacacokinetic and pharmacodynamic parameters of the drug by decreasing the side effects, enhancing the stability, prolongs the drug release and reducing the dosage frequency. Finally, these review highlights the effective use of various nanoparticles in treatment of Breast cancer, with their enhanced safety and efficacy.

KEYWORDS: Breast cancer (BC), Nanoparticles, anti-cancer medications.

INTRODUCTION

One of the serious illnesses that have been killing people in recent years is cancer. Breast cancer (BC) is the most common cause of death for women of all cancer types.[1] According to the global cancer statistics of 2022, breast cancer holds the top position in both female incidence rate(24.5 %) and mortality rate (15.5 %).[1] There are several subtypes of BC, including triple-negative, HER2-/HER2+, luminal A-like, and luminal B-like (HER2-/HER2+). In the treatment of BC, well-established and often employed therapeutic

approaches include surgery, chemotherapy, radiation, targeted therapy, and endocrine therapy. However, a few side effects of these traditional remedies prevented them from being widely used in clinical settings.[2] Consequently, the implementation of new and more potent treatments is urgently needed. One such treatment is the use of drug-coated nanoparticles (NP), which are presently the subject of extensive research.[3]

Submicron (100–1000 nm) particles are known as nanoparticles, and they are typically created from substances including polymers, lipids, viruses, and inorganic compounds.[4] The nanocarriers need to be composed of a biocompatible substance, be easily functionalised, have a good characterisation, be soluble, have the capacity to circulate for a long time, not aggregate, and have a high absorption efficiency by the target cells. According to the materials they are composed of, nanocarriers can be divided into three groups: (1) lipid-based, (2) polymeric, and (3) inorganic.[4] Scientists are interested in nanoparticles because they can be used in a single system for cancer treatment, medical imaging, and diagnosis.[5] Higher drug loading and better drug release properties are made possible by designing nanoparticles with a high surface area-to-volume ratio. Furthermore, targeting molecules on the surface of nanoparticles can be altered to bind to particular cells alone, boosting a drug's effectiveness and specificity.[6] Furthermore, using drug release mechanisms driven by variables like pH, redox potential, enzyme presence, or temperature, nanomaterials might improve the deposition of nanomedicines precisely to the site of sickness.[7]

According to certain studies, nanomaterials can be directed against the tumour blood vessel endothelial cells, releasing anti-angiogenic medications, effectively inhibiting the formation of tumour blood vessels and lowering the oxygen supply.[8] Nanotechnology may hold the key to improving the targeting capabilities of current treatments, enhancing localised medication efficacy, reducing systemic toxicity, boosting imaging, improving diagnostic sensitivity, and improving radiation therapy.[9]

Medication delivery has been profoundly impacted by recent developments in nanotechnology, especially in the pharmaceutical sector. Therapeutic drug delivery that is precise and targeted has become possible because to nanocarriers, which include nanoparticles. The design of these nanoparticles for drug delivery incorporates nanocomposites including polymers, liposomes, carbon nanotubes, silver nanoparticles, nanorods, and gold nanoparticles.[6]

S. No	Drug	Polymer	Mechanism of action	Reference
1.	Palcitaxel	PEG-b-poly(D,L-lactic acid) (PEG-PLA)	By binding the tubulin β-subunit, it prevents microtubules from functioning normally. It results in tubulin polymerization, which throws off the order of cell division and kills cells. It stops mitosis and cell cycle progression, which in turn stops cancer cells from growing.	[10, 9]
2.	Xanthone	PLA(poly lactic acid)	By causing macrophages to produce nitric oxide, they impede the lining of tumor cells.	[10]
3.	Nitrocamptothecin	PLGA	The enzyme topoisomerase-I is their target. Rapid pH-dependent hydrolysis transforms the structure of 9-nitrocamptothecin and its related analogs from closed ring lactone to inactive hydroxyl carboxylate, resulting in a loss of anticancer action.	[10]
4.	Etoposide	PLGA and Pluronic F68 NPs	This medication produces compounds that attach to DNA and damage it by inhibiting topoisomerase-II.	[10]
5.	Doxorubicin	PLGA	Interfere with the production of nucleic acids, resulting in growth arrest and programmed cell death.	[7 &14]
6.	Cisplatin	PLGA and mPEG NP	By attaching itself to the purine residue of tumor cell DNA, it prevents cell division and eventually triggers apoptosis, which kills the cell.	[10]
7.	Ixabepilone	PLGA	Blocks cancer cells during the mitotic phase of the cell division cycle by stabilizing the dynamics of microtubules. Eventually, this leads to cell death and apoptosis.	[7]
8.	Olaparib	PLGA	Cells without functional BRCA1 or BRCA2 become inactive when PARP1 and Poly (ADP-ribose) polymerase 2 (PARP2) are inhibited, which increases genomic instability	[7]

			and causes cell death. Olaparib and talazoparib are two PARP inhibitors.	
9.	Hypericin	Gold nanoparticle	As a photosensitizer, hypericin can kill cancer cells through necrotic, autophagic, or apoptotic pathways. Hypericin is applied directly to the tumor site or systematically through the circulatory system in photodynamic therapy. The generation of ROS results in oxidative damage to the cell's internal components, which ultimately destroys cancer cells.	[15]
10.	Docitaxel	Poly(ethylene glycol)-block-poly(ε −caprolactone) methyl ether	Act by disrupting the microtubular network in CELLS	[7]
11.	Tamoxifen	polyvinyl pyrrolidine (PVP), polyacrylicacid, polystyrene,	When an anti-estrogen, or selective estrogen receptor modulator (SERM), binds to an estrogen receptor in BC cells, it inhibits the hormone's effects.	[16&17]
12.	Tetrahydro-cannabinol	Gold nanoparticles	Reduced growth of cancer cells through the pro-apoptotic p8-ATF-4TRIB3 pathway being induced.	[15]
13.	B- sitosterol	PLGA,PEG AND PLA	The antiproliferative activity of β-Sit against MCF-7 and MDA-MB-231 cells was increased by encapsulating it in PLGA nanoparticles in a concentration-dependent manner compared to the control groups. This could be a potential approach to increase the therapeutic efficacy of β-Sit against cancer.	[11]
14.	Palcitaxel	Poly ethoxylatedcastoroil(Cremophor)	By binding the tubulin β-subunit, it prevents microtubules from functioning normally. It results in tubulin polymerization, which throws off the order of cell division and kills cells.	[18&10]
15.	Docitaxel	PLGA and PEG	Act by disrupting the microtubularnetwork in Cells.	[18&7]

16.	Doxorubicin	POLY(methacrylic acid)	Disrupt nucleic acid synthesis, thereby causing growth arrest and programmed cell death	[18&7]
17.	Curcumin	PGMD (poly-glycerol-malic acid-dodecanedioic acid)	Cur-NPs enhanced tumor apoptosis and necrosis, suppressed cancer cell growth, and dramatically decreased tumor volume and weight.	[19&20]
18.	Curcumin; doxorubicin (pH-sensitive)	PLGA, Polyethylene glycol,	Cur-NPs enhanced tumor apoptosis and necrosis, suppressed cancer cell growth, and dramatically decreased tumor volume and weight.	[18,19&7]
19.	Gallic acid	Poly ethylene glycol or PVA	Gallic acid complexes can be actively targeted by conjugating targeting ligands on their surface, magnetically steered to specific tissues using external magnets, or they can simply diffuse to tumor areas because of the enhanced retention and permeability (EPR) effect. Gallic acid-IONPs are designed to release the medications in reaction to the tumor microenvironment (TME), such as an acidic pH, or with the aid of a magnetic field once they have reached the target tissues.	[17]
20.	Palcitaxel with trastzumab	PLGA	The HER family of receptors plays a key role in the pathophysiology of a number of malignancies by controlling cell survival, proliferation, and differentiation via a variety of pathways. A humanized monoclonal antibody called trastuzumab targets breast cancer cells' overexpressed HER2 receptors.	[21]
21.	Siakosaponin D	poly (latic-co-glycolic acid)	The macrophage membrane-biomimetic NP loaded with saikosaponin D showed increased cell endocytosis, immunological evasion, and selective accumulation, indicating targeted selectivity to cancer cells. Additionally, through the angiogenic	[22]

			pathway's VEGFR, AKT, and ERK, SCMNPs successfully prevented breast cancer tumor growth and metastasis both in vitro and in vivo.	
22.	Campothecin	Hyaluronic acid	Camptothecin (CPT) has been demonstrated to have the most potent cytotoxicity for tumor cells in both the S and G2 phases of the cell cycle. When combined with immune checkpoint inhibitor antiPD-L1 immunotherapy, chemo-photothermal therapy with polypyrrole-loaded hyaluronic acid NPs synergistically enhanced the anti-tumor immune response, eliminating primary breast cancer and preventing tumor metastases and recurrences in 4T1 tumor-bearing mice.	[23]
23.	Argonaute 2 (AGO2) protein	polyethylene imine (PEI), cationic dendrimers, Chitosan/poly (lactide-*co*-glycolide) (PLGA).	MicroRNA apparatus Argonaute 2 (AGO2) protein, a component of the RISC complex, functions as a delivery system and a stabilizing agent for microRNA. AGO2 protein-conjugated, anti-HER2 antibody-linked, and fuorophore-tagged Super permanganate iron oxide (SPION) nanoparticles (SP-AH nanoparticles) were created in this work and employed as a vehicle for MIR376B, an autophagy-inhibiting microRNA. These functionalized nanoparticles effectively inhibited autophagy and delivered a significant quantity of the microRNA to HER2-positive breast cancer cell lines both in vitro and in vivo using a xenograft nude mouse model of breast cancer.	[24]
24.	Rhodium II citrate [Iron oxide nanoparticles]	Oleic acid, poly ethylene glycol, poly vinyl alcohol	In Balb/c mice with orthotopic 4T1 breast cancer, rhodium II citrate INOP (iron oxide	[17]

			particle) complexes significantly decreased tumor volume and increased tumor necrosis. Although these NP complexes were not harmful to the mice, they were able to efficiently decrease tumor volume because of their efficient transport, accumulation, and citrate-induced suppression of glycolysis.	
25.	Eribulin		causes apoptotic cell death by alternatingly inhibiting the microtubule growth phase.	[7]
26.	Rapamycin	Hyaluronic acid, CD44-tropic (ligand), 3- amino-4-methoxy-benzoic acid	Drug delivery to CD44-positive breast cancer cells that is localized, maintained, and regulated to treat cancer	[17]
27.	Chondroitin sulfate	Albumin corona nanoparticles	Bovine Serum Albumin (BSA) and Chondroiyin Sulfate (CS) have a dual effect that causes BC-DOX-NPs (Bovine and Chondroitin Doxorubicin nanoparticles) to interact with the gp60, SPARC, and CD44 receptors on tumor cells. This enhances their uptake and accumulation within tumor tissues and allows BC-DOX-NPs to target CD44 effectively, which results in higher cellular uptake and cytotoxicity against 4T1 cells than either CS-DOX-NPs or free DOX.	[12]
28.	Rapamycin and piperidine	PLGA	Piperidine and rapamycin together may have the benefit of preventing P-glycoprotein efflux and enhancing drug uptake in cancer cells, which would increase rapamycin's anticancer effectiveness. Additionally, piperidine's natural ability to combat cancer cells offers the benefit of a synergistic effect on the tumor.	[13]

Because of their various benefits and extreme adaptability, nanomaterials can enhance cancer detection and treatment. However, the possible benefits must be evaluated against aspects like production cost, scalability, safety, and complexity of nanoformulations.[9] Using nanoparticles in nanotechnology presents a possible approach to treating TNBC. The function of nanoparticles in TNBC has been the subject of numerous investigations to date. Inducing apoptosis, lowering chemotherapeutic drug adverse effects, improving drug entrapment effectiveness, and eventually increasing bioavailability are all accomplished using nanoparticles.Nanotechnology developments can be used to target certain molecular markers in cancer cells, improving the efficacy of treatment while reducing damage to healthy cells.[25]

Two documents about the use and status of nanotechnology, the risk-based framework, specific guidelines for conducting clinical and nonclinical trials, manufacturing quality and controls, and environmental considerations were released by the FDA.[9] In addition to avoiding the problems associated with traditional breast cancer treatments, the combination of photosensitizers with multifunctional organic nanoparticles can enhance the use of intractable, poisonous, or unstable photosensitizers. The MNP is especially well-suited for the intramoral use of magnetic materials. This method could be used to treat breast cancer, especially in its early stages when there are just one tumor and no lymph nodes are present. Because the nanoparticle platform offers special advantages, using nanoparticles in combination therapy may increase the benefits of this type of therapeutic approach.

CONCLUSION

Nanomedicines have shown enhanced drug uptake and retention in the treatment of breast cancer, leading to more effective tumour tissue targeting and decreased systemic toxicity. Nanotubes, gold nanoparticles, magnetic nanoparticles, iron oxide nanoparticles, solid lipid nanoparticles, and other nanoparticle formulations are employed. Drug delivery, release, and targeting could all be significantly enhanced by nanotechnology, thereby increasing therapeutic effectiveness and reducing adverse effects. Drugs that target nanomaterials may benefit patients with breast cancer and mark a significant advancement in the disease's detection and management. In the near future, nanotechnology for cancer diagnostics, chemotherapy, and radiation therapy is expected to advance significantly, making the cancer landscape much more manageable for both patients and doctors.

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