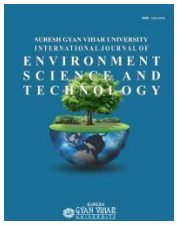

SGVU International Journal of Environment, Science and Technology

E-ISSN: 2394-9570

Vol.9 Issue 1 Page No 1-10

***Research Article*:**

ROLE OF NANOBIOTECHNOLOGY TO COMBAT BREAST CANCER

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Keywords

Breast cancer

Nanocarriers,

Nanomedicine,

Nanotoxicity

Abstract

Amongst the assorted forms of cancer, breast carcinoma could be an extremely heterogeneous malady and referred to as the leading explanation for death among women globally. The intensive knowledge domain investigation in engineering and cancer medicine analysis has been evolved over the years for its effective treatment. However, the arrival of chemotherapeutical resistance in breast cancer is one in all the most important confront researchers face in achieving productive chemotherapy. Analysis within the space of cancer nanotechnology over the years have currently been revolutionized through the event of smart polymers, lipids, inorganic materials and eventually their surface-engineering with targeting ligands. Moreover, nanotechnology further extended and brings within the notice the new theranostic approach that combining the medical care and imaging simultaneously. Currently, analysis is being envisaged in the space of novel nano-pharmaceutical construct like liposome, nanotubes, dendrimers, solid-lipid nanoparticles, quantum dots, which focuses to form the therapy curative and long-lasting. The recent advancement of various surface-engineered/targeted nanomedicines improved the drug effectuality in breast carcinoma. Toxicological profiling of these nanostructures should be done before their release into environment. Great collaboration among experts in academia, researchers and pharmaceutical sector is needed for the further development of breast cancer treatment modalities.

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Introduction

Breast cancer is a heterogeneous disease with alarming cancer incidence and mortality. Across the globe 19.3 million new tumor cases and 10.0 million cancer deaths had observed till 2020. Among the global burden of cancer, breast cancer in women has been noticed to be more than 24% with higher incidences of associated mortality (Asghari et al., 2019; Sung et al., 2021). It is the second most common reason of mortality from cancer among women in the world. Breast cancer always evolves silently. Patients discover their disease usually at the time of routine screening as well as may accidentally find lump in breast with or without changes in shape or size or nipple discharge. However, mastalgia is not uncommon. To diagnose breast cancer tissue diagnosis is must along with physical examination and imaging (especially mammography). The survival rate improves with early diagnosis. The tumor tends to spread through lymphatics as well as hematogenous responsible for locally advanced tumor and distant metastasis of the tumor respectively and hence carries poor prognosis. This explains and emphasizes the importance of breast cancer screening programs (Alkabban & Ferguson, 2022).

Due to non-availability of advanced selective medical care for triple negative breast cancer, the subtype is managed with standard medical specialty as well as removal of growths by surgery, typically together with therapy and localized therapy (Fig. 1). However, associated witness toxicities to traditional tissues and relapse when treatment has been the limiting issue (Bromma et al., 2020). Using the targeted approach of drug delivery may considerably increase the therapeutic gain by lowering the harm to normal cells. Further, heterogeneousness of the tumor poses the restriction on the utilization of single therapeutic agent, which may confiscate the full tumor. Thus there's an utmost need for tumor prevention and controlled targeted ways to scale back carcinoma associated morbidity and mortality (Harris et al., 2019). Biological drugs, targeted treatment and gene therapy can doubtless reduce the mortality of patients with breast cancer (Al-Mahmood et al., 2018). Intrinsic limitations of cancer therapies inspired the intervention of applied science in drug development to boost the therapeutic effectualness and safety that is said as cancer nanomedicine (Afzal et al., 2021). Various application of nanomedicines in targeted drug delivery, diagnosis, and imaging and therapeutic has the potential to fulfill the requirement of cancer diagnostics and therapeutic system (Teles et al., 2018).

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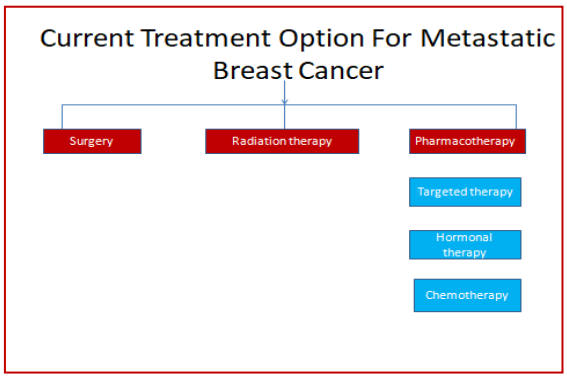

Figure 1: Recent therapeutic options for breast cancer (Al-Mahmood et al., 2018)

Mechanism of action of nanomaterials

Nanomaterials target the malignant neoplastic disease cells by biomimetic methodology while not harming normal healthy cells (Harris et al., 2019). In 2005, the primary nanoformulation Abraxane® got approval as medical specialty for pathologic process carcinoma. Subsequently numerous nanotherapeutics are being used with nice efficacy (Gradishar et al., 2005). Multiple nano-formulations are designed and investigated as a region of targeted strategy for breast cancer management. Nanoparticles have the potency to hold therapeutic molecules and deliver them to targeted growth location. It may also serve the aim of each diagnosing and treatment of breast cancer (Singh et al., 2017). Nanoparticles targets tumors either by passive targeting or by active targeting. Thanks to leaky vasculatures, growth tissues have increased permeableness and retention, referred to as EPR impact. Nanoparticles take the benefits of EPR effect and diminished removal from the bodily fluid system. It gets accumulated within the tumor site, releases the drug and induces apoptosis; this is often known as passive targeting. Whereas, in active targeting, protein-based targeting parts like antibodies and RGD (arginylglycylaspartic acid) peptides are adscititious to the nanoparticles to boost their orienting to specific tumor site. Active targeting takes advantage of the ligand-receptor affinity. It targets the extremely expressed surface receptors on tumor cells with their contrast specific ligand connected to the nanoparticles (Hejmady et al., 2020; Raj et al., 2021). The addition of imaging agent to the nanoparticle provides complete details regarding its path, binding and unleash of the drug. The nano sized agents designed for the aim of each diagnosing and medical care are referred to as theranostics (Mohammadpour & Majidzadeh-A, 2020). They are drug delivery systems integrated with molecular or targeted imaging agents (Hapuarachchige & Artemov, 2020).

Importance of nanomaterials in breast cancer

Nano-biotechnological approaches have improved the clinical outcome of breast carcinoma management and treatment. It conjointly resulted in wide understanding of tumor nature, characteristics and its

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atmosphere that results in customized treatment choices for various intrinsic subtypes of breast cancer (Gonciar et al., 2019; Santosh Kumar Singh, Shriti Singh, James w Lillard Jr, 2017). Nanobiotechnology ensures to overcome the challenges faced by conventional breast cancer treatments (Table 1). Nanostructures play a superb role in tumor designation and targeted drug. the explanations behind this are very little size, high surface-to-volume ratio, tunable physicochemical properties, higher load carrying skills (Jawahar et al., 2020), longer circulation time, high uptake and retention of nanostructures (Bromma et al., 2020), unharness of the loaded drug at property rate (Biancacci et al., 2020), bioavailability, biocompatibility (Sohail et al., 2020), and escape from p-glycoprotein pump (Sharmiladevi et al., 2021). These unmatchable properties of nano enabled structures brought the revolutionary modification in breast carcinoma prognosis and treatment efficacy.

Table 1: A list of the few key challenges to breast cancer chemotherapy and the solutions provided by nanobiotechnology (Wu et al., 2017)

Challenges to breast cancer chemotherapy	**Solution by nanobiotechnology**
Non specific targeting	Nanocarriers ensures specific targeting of therapeutics to tumor site
Unable to remove tumor stem cells	Passive targeting and active targeting to tumor stem cell
Insufficient access of drug to brain and bone tissues	Sufficient access of nanodrug to these tissues
Drugs have disadvantage of low aqueous solubility and stability inside the body	Nanocarriers mediated delivery can achieve high drug solubility and stability

Application of nanomaterials in breast cancer

According to global cancer statistics until 2020, female breast cancer as the most commonly diagnosed tumor, with approximately 2.3 million new cases. Its incidence is rising at a great pace with high mortality rates (Arnold et al., 2022; Sung et al., 2021). Therefore, targeted treatment option with early diagnosis is highly needed for breast tumor management. Thanks to Nanomaterials for satisfying the current need and improved the quality of life of breast tumor patients (Mohammadpour & Majidzadeh-A, 2020). For this nano enabled

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carriers play utmost important role like metallic nanoparticles, liposomal and solid-lipid nano-structures, carbon dots, quantum dots and nanodiamonds etc (Banthia et al., 2022).

Nanomaterials application in breast cancer can be widely categorized in (i) imaging (ii) drug delivery and (iii) theranostics. Therapy and diagnosis of tumors simultaneously leads to theranostics (Avitabile et al., 2018). Various therapeutic agents in targeted drug delivery or in combination lead to theranostic nanostructures. These drugs comprise Doxorubicin, Resveratrol, Trastuzumab, herceptin, paclitaxel (PTX), dextran, curcumin, tamoxifen, methotrexate. In a study Mamnoon et al., delivered estradiol-conjugated hypoxia responsive polymeric nanoparticles. These nanoparticles with the drug Doxorubicin is targeted to the spheroid cultures of MCF-7 breast cancer cells. It exhibited high cytotoxicity, higher cytosolic and nuclear internalization (Mamnoon et al., 2020).

Paclitaxel and piperine (PTX-PIP) co-loaded targeted liposomes had demonstrated higher cytotoxicity and superior uptake in MDA-MB-231 cells. It also proved the synergistic antitumor effect of PIP (Burande et al., 2020). In another study lysin decorated solid lipid nanoparticles of Epirubicin exhibited remarkable anticancer effects and cytotoxicity to MCF-7 breast cancer cell line as compared to pure drug (Bayat et al., 2021).

Nanotoxicity and Regulatory Challenges

Advances in smart technologies such as nanotechnology and biotechnology have achieved the re-construction of existing materials and converting into novel nano-range products that can function beyond the limits of traditional techniques. With the advancement within the distinctive properties and functionalities of these novel nanostructures broaden the arrays of applications; it additionally imply for structural modifications to existing safety assessment processes (Umapathi et al., 2021). After a decade the requirement to switch existing risk management practices to incorporate nano-specific behaviors and exposure pathways was recognized, relevant policies for evaluating, and dominant health risks of nano-enabled materials continues to be lacking (Sarma et al., 2021).

This issue is long accepted and recognized but still unresolved problems associated with nanomaterials toxicity concern and safety. Nanomaterials from various sources and industries like paints, cosmetics products, fabrics and various health care products allowed them to enter into environment. Intentional and un-

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intentional release of nanostructure should be taken care to avoid their entry into water, air and land resources (Leonel et al., 2021). Inattentive release of nanomaterials into environment poses a great risk to human and wild life. Researchers showed that respirable nanoparticles of carbon nanotubes and small nano aerosol enter into the human body. It can cause respiratory problems, lung diseases and other tissues toxicity. Numerous nanomaterial such as fullerene, quantum dots and nano silver affect human health and environment (Das et al., 2021). The toxicity of each nanomaterial should be accessed carefully to predict their impact on environment. Fate of nanomaterials, their structure and reactivity should be considered appropriately before their release into the environment. Nanotoxicity is lagging behind due to unavailability of suitable detection and characterization techniques. These challenges include avant-grade design, equitable methods in evaluating toxicity and direct impact on human life and environment. Toxicological profiling of nanoparticles and knowledge of structure-activity-fate relationships of nanosubstances will help to develop strategies to minimize nanotoxicities and maximize their benefits to environment and mankind (Nagy & Robbins, 2019; Saleh, 2020).

Conclusion and future prospects

Tunable characteristics and high surface area to volume ratio of nanomaterial make them potential candidate for biomedical platform. Various nanostructures like gold nanoparticles, silver nanoparticles, fullerene, iron oxide and zinc oxide nanocomposites find their way to serve mankind and provide platform for hyperthermia and immunotherapy. Various nanoforms like nanocages, nanorods, nano stars, nanoflower and nano shells have been implicated in photothermal treatment for breast cancers. Gold and iron nanostructures mark their potential on combinational therapy with photothermal therapy as well as in cancer antigen and immune adjuvant delivery (Aminabad et al., 2019; Liu et al., 2018; Magro et al., 2018). Biocompatible and non-toxic metallic nanoparticles can be manipulated and modified according to the need, it can easily be functionalized with various nanocarriers (liposomes, quantum dots, dendrimer), antibody and even with drug molecule to make targeted drug delivery possible. It selectively releases the drug at targeted location and reduces the destructive effect on healthy cells. This is boon for various difficult to treat diseases. New abilities make it feasible to diagnose a cancer and at a same time to treat it with a nanodrugs molecule. This theranostic

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application is only possible because of designing of unique nanomaterials. A proper study of pharmacokinetics of nanomaterials is required to ensure risk assessment and safe nanomedicine applications (Klochkov et al., 2021; Pindiprolu et al., 2018). Designing novel nano-formulations without causing any adverse effects to human health and environment is of critical importance. To fulfill these requirements a great collaboration among experts in oncology, pharmacokinetics, toxicology and immunology is prerequisite for development of breast cancer nanomedicine in future.

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