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REVIEW ON NANOTECHNOLOGY USE IN BREAST CANCER TREATMENT

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ABSTRACT
Breast cancer (BC) is the most common type of cancer affecting women worldwide. Triple-negative breast cancer (TNBC) lacks the three primary receptors—estrogen, progesterone, and human epidermal growth factor receptor-2 (HER2). The absence of these hormonal receptors in breast cancer cells is associated with aggressive behavior and a higher tendency for metastasis, which often leads to resistance to chemotherapy. Although several treatments and therapies are available to control the spread of BC and TNBC, they can also cause side effects that damage healthy cells and tissues. Nanotechnology focuses on the physical and biochemical characteristics of nanoparticles used in drug applications. The goal of targeted nanoparticle drug delivery is to minimize the side effects of anticancer drugs while reducing both dosage requirements and treatment costs, which are major limitations of traditional cancer therapies. The present review highlights various types of nanoparticles and their applications in breast cancer treatment.

KEYWORDS - *Nanoparticles , Breast Cancer , Nanotechnology, Ductal Carcinoma, Lobular Carcinoma ,Liposomes,Micelles, Etc*

INTRODUCTION

Cancer remains one of the biggest public health challenges worldwide, ranking as the second leading cause of death. According to the National Center for Health Statistics in the United States, around 1.8 million new cancer cases and over 600,000 related deaths were recorded in 2020 alone [1]. In 2015, the World Health Organization (WHO) estimated that cancer was the first or second leading cause of death before the age of 70 in 91 out of 172 countries. In another 22 countries, it ranked as the third or fourth leading cause of death [2]. Although many surgical and therapeutic options are available for treating cancer, traditional methods such as chemotherapy remain highly toxic and often cause serious side effects. The lack of selectivity and systemic toxicity associated with conventional chemotherapy limit its effectiveness and safety [3]. To overcome these limitations, researchers have turned their attention to nanotechnology and its growing potential in improving cancer treatment[4]. Nanotechnology is widely used to design and develop various nanomaterials, such as nanoparticles [5]. It is one of the rapidly evolving technologies that creates new possibilities for diagnosing and treating human cancers [6]. Nanotechnology is also opening new paths for cancer research, allowing scientists to explore and understand cancer at the molecular level. According to the American Society for Testing and Materials (ASTM), it involves designing, producing, and analyzing systems or devices whose shape and size are adjusted within the nanometer scale, typically between 1 and 100 nanometers, across two or three dimensions. The word "nano" comes from the Greek term for "dwarf," which refers to something extremely small in nature [7]. The idea of nanomedicine was originally suggested by Nobel Prize-winning physicist Richard P. Feynman in 1959, when he imagined creating tiny machines that could be placed inside the human body to carry out tasks at the cellular or molecular level. Today, many methods using nanoparticles are actively being explored, bringing a wide variety of new possibilities to healthcare and medicine [8].

Many types of nanomaterials have been tested in clinical trials, and several have received approval from the U.S. Food and Drug Administration (FDA) for use in cancer treatment. These include both organic and inorganic materials. Inorganic nanoparticles made from metals such as gold, silver, and chromium are being produced on a large scale. Similar to albumin-bound paclitaxel nanoparticles used for treating metastatic breast cancer, these metal-based nanoparticles can also be coated with proteins to enhance their effectiveness [9,10]. Albumin-bound nanoparticles became the first chemotherapy-based nanodevices to receive FDA approval in 2005 [11].
The main aim of nanomedicine is to achieve accurate diagnosis and effective treatment with minimal side effects, while also assessing how well noninvasive therapies work.

Breast Cancer

In 2005, cancer surpassed heart disease as the leading cause of death among people under 85 in the United States (Jemal et al., 2007). Although significant advances have been made in understanding how cancer develops and progresses, as well as in creating targeted therapies, breast cancer continues to show high rates of occurrence and mortality worldwide.Since 1990, breast cancer rates

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have risen by about 1.5 percent each year [12]. Diagnosis typically starts with self-examination, clinical breast exams, and imaging methods such as mammography, PET scans, and MRI, followed by a biopsy to confirm whether the disease is invasive. The introduction of mammography has greatly improved early detection, and large clinical studies show that annual screening for women aged 50 to 69 can reduce breast cancer deaths by around 30 percent (Elwood et al., 1993; Kerlikowske, 1997). While early detection often means less invasive surgeries and better survival rates, the outlook for advanced, metastatic breast cancer remains poor, with a five-year survival rate still below 15 percent [13,14]

Types of Breast Cancer

1. Ductal carcinoma -"It starts in the milk duct and is the most common type."
2. Lobular carcinoma -"This one starts in the lobules. Invasive breast cancer happens when cancer cells break out from the lobules or ducts and spread into nearby tissue, raising the risk of it traveling to other parts of the body" [15].

Symptoms of Breast Cancer

"Early signs of breast cancer often include a thickened area in the breast or a lump there or in the armpit Catching it early boosts your chances of recovery."
"Other symptoms can include:

1. Pain in the armpits or breast that doesn't come and go with your monthly cycle
2. Pitting or redness on the breast skin, kind of like an orange peel
3. A rash around or on one nipple
4. Discharge from the nipple, sometimes with blood
5. A sunken or inverted nipple
6. Changes in breast size or shape
7. Peeling, flaking, or scaling on the breast or nipple skin
8. Most lumps aren't cancer, but it's smart to get them checked by a doctor" [15].

Stages of Breast Cancer

"Doctors stage breast cancer based on the tumor's size and whether it's spread to lymph nodes or other parts of the body. There are a few ways to do this—one common method runs from stage 0 to 4, with possible sub-stages in between."
Stage 0:- "Known as ductal carcinoma in situ (DCIS), the cells stay confined within a duct and haven't invaded the surrounding tissues."
Stage :- "The tumor is no bigger than 2 cm and it hasn't reached any lymph nodes yet at this early stage."
Stage 2:- "The tumor measures about 2 cm and has begun spreading to nearby lymph nodes."
Stage 3:- "The tumor is up to 5 cm across and might have spread to some lymph nodes."
Stage 4:- "The cancer has spread to distant organs, especially the bones, liver, brain, or lungs."



Fig: 1 Stages of Breast Cancer

Using Nanotechnology In cancer

The idea of nanotechnology was first introduced by an American physicist in 1959. Thirty years later, in 1989, scientists managed to manipulate matter at the atomic level by arranging individual atoms. However, nanotechnology officially came into existence around 1990. It was developed as a way to control and observe molecules and atoms ranging in size from about 0.1 to 100 nanometers [16].

Nanomaterials differ from larger, bulk materials in their chemical and physical properties. They typically have a greater ability to speed up chemical reactions, stronger adsorption capabilities, more active surface reactions, and a much larger surface area. In addition, nanomaterials also show several other properties, such as faster diffusion, greater reaction activity, and lower melting points [17]. Nanomedicine emerged from the combination of nanotechnology and medicine. Through the use of nanotechnology, it

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became possible to study and understand biological information at the level of individual molecules [18]. Nanoparticles are generally divided into two main types. The first type is made mostly from organic molecules, while the second type usually has metals or minerals at its core.

Nanoparticles types and the treatment of breast Cancer

In recent years, nanotechnology has advanced quickly, leading to the development of several important cancer treatment approaches. For breast cancer, some of the most commonly used nanoparticles include liposomes, micelles, polymeric nanoparticles, solid lipid nanoparticles, and gold nanoparticles.

Liposomes

Liposomes were first created in 1964 by Bangham and Horne. They are small, spherical vesicles measuring about 50 to 200 nanometers in size, made up of an aqueous core surrounded by a phospholipid layer. Because this layer is biocompatible, biodegradable, and non-immunogenic, liposomes are widely used to deliver both water-soluble and fat-soluble drugs directly to target sites in the body. Their tiny size allows them to pass easily through blood vessel pores and gather in tumor tissues[19]. Research has also shown that when P-glycoprotein (P-gp) activity is blocked by anionic membrane lipids and liposomes carrying rhodamine 123—a known P-gp substrate—are introduced, rhodamine retention increases in MCF-7/P-gp cells. This indicates that P-gp plays a role in transporting its substrates. Examples of liposomes used for delivering anticancer drugs to breast cancer cells are The first liposomal drug, a formulation of doxorubicin known as Doxil®, was approved by the FDA in 1995 for treating ovarian cancer, AIDS-related Kaposi's sarcoma, and multiple myeloma. It was later approved for use in breast cancer treatment as well. Another formulation, a paclitaxel-loaded nanoliposome made with phosphatidylcholine and cholesterol, was tested on MCF-7 breast cancer cells. The findings revealed that this liposomal version of paclitaxel killed significantly more cancer cells than the free drug alone [20,21].



Figure No 2: Liposomes

Micelles

Micelles are tiny particles, typically ranging from 10 to 100 nanometers in size, formed through the self-assembly of amphiphilic molecules that have water-loving heads and water-repelling tails. They offer several benefits, including longer circulation time in the bloodstream, low toxicity, and better accumulation in tumor tissues. Because of these properties, micelles are often used to deliver anticancer drugs that do not dissolve well in water. Many anticancer drugs have been enclosed in micelles to improve their delivery to breast cancer cells. In one study, Batrakova and colleagues found that exposing cells to Pluronic P85 caused a significant reduction in ATP levels specifically in multidrug-resistant (MDR) cells, marking the first time this effect was observed. Moreover, the uptake and distribution of micelles within MCF-7 breast cancer cells and tumor tissues were higher compared to those of the commercial drug. In addition, micelles showed good safety, with a maximum tolerated dose of 50 mg/kg—about 2.5 times higher than that of the commercial drug, which was 20 mg/kg[22]

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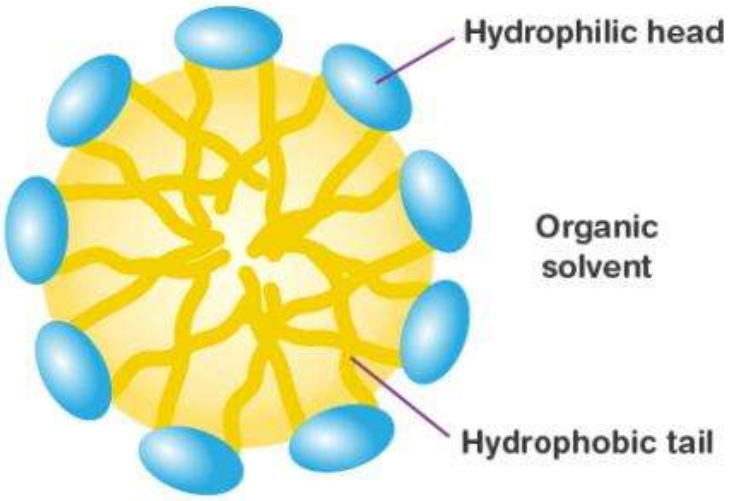


Figure No 3: Micelles

Polymeric Nanoparticles

Polymeric nanoparticles have been designed to serve as nanocarriers for hydrophobic chemotherapeutic drugs and hormone regulators, including agents like taxanes, camptothecin, cisplatin, and tamoxifen[23].Polymeric nanoparticles, such as polymeric micelles, capsules, colloids, and dendrimers, are core–shell structures formed through the self-assembly of amphiphilic and biodegradable polymers in aqueous solutions. Common examples include poly(D,L-lactic acid), poly(D,L-lactic-co-glycolic acid), poly(ε-caprolactone), and their PEG-based copolymers, where PEG is typically used to prevent particle aggregation[24]. Conjugating with targeting molecules like peptides and antibodies improves the delivery of therapeutics to cancer cells[25,26].A key feature of polymeric nanoparticles is their ability to release drugs in a controlled way, not just through diffusion or swelling of the nanostructure, but also by responding to environmental changes like variations in pH [27]. Temprature [28]. Genexol®-PM, which contains paclitaxel incorporated into poly(D,L-lactic acid), is a polymer-based nanomedicine currently undergoing clinical trials for the treatment of breast cancer [29].In a Phase II clinical trial evaluating Genexol-PM for metastatic breast cancer, 41 patients received an intravenous dose of 300 mg/m² over a three-hour period every three weeks. The treatment showed an overall response rate between 43.5% and 73.7%, with a median disease progression time of about nine months.The reduced toxicity and fewer side effects may be due to the absence of Cremophor EL (polyoxyethylated castor oil), a solvent normally used to enhance paclitaxel's solubility but known to cause hypersensitivity reactions and nerve damage [30].Although polymeric nanoparticles work well as drug carriers for hydrophobic chemotherapeutic agents and hormone regulators, they still have certain limitations [31].

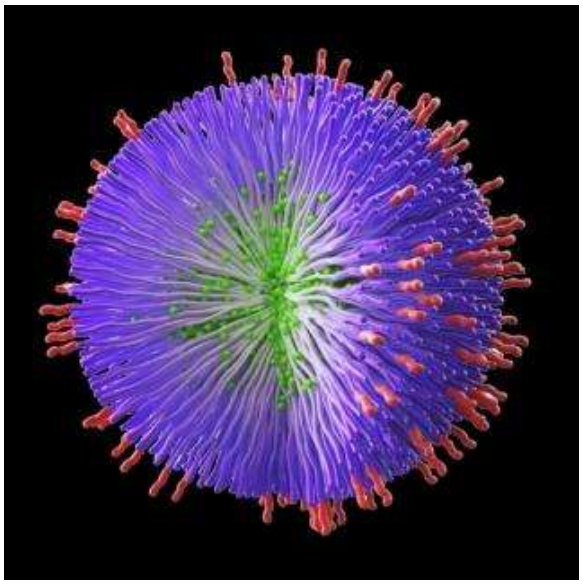


Figure No 4: Polymeric Nanoparticles

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Solid Lipid Nanoparticles (SLNS)

Solid lipid nanoparticles (SLNs) were first introduced as a new oral drug delivery system (Mehnert and Mäder, 2001). Over time, they have gained significant attention for cancer therapy due to their many advantages, such as controlled drug release, biocompatibility, high drug-loading capacity, and excellent physical stability. SLNs represent an advanced type of colloidal carrier system that can help improve the effectiveness of anticancer drugs[32]. By combining SLNs with anticancer agents, it is possible to overcome drug resistance, increase the concentration of drugs within cancer cells (including breast cancer cells), enhance antitumor activity, and reduce damage to healthy cells. These nanoparticles can also be absorbed by cells through endocytosis or phagocytosis, allowing the encapsulated drug to enter the target cells (Güney and Kutlu, 2011). Because of these benefits, SLNs are often used as alternatives to other delivery systems like liposomes or polymeric nanoparticles that have certain limitations [33].

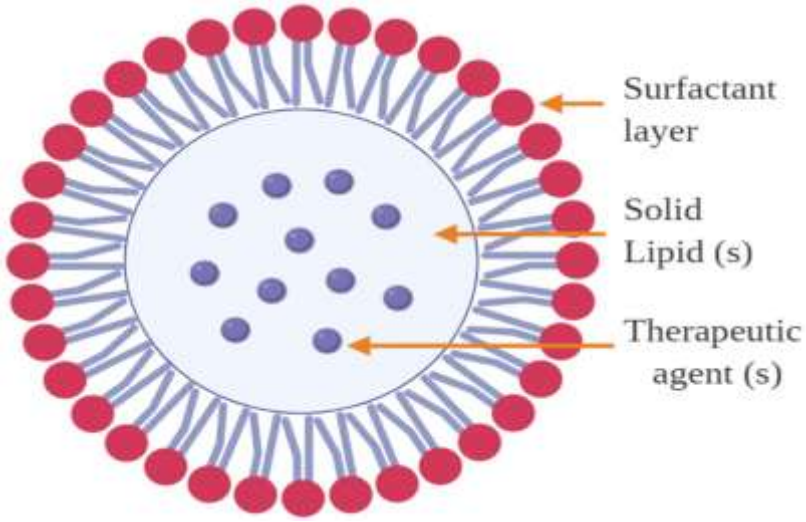


Figure No 5 : Solid Lipid Nanoparticles

Gold Nanoparticles

Gold nanoparticles (AuNPs) are being explored for use in clinical diagnosis, biomedical imaging, and the treatment of solid breast tumors. They are also being studied for their potential roles as contrast agents, photothermal therapy agents, drug delivery systems, and radiosensitizers [34,35]. Gold nanoparticles are provided as a suspension containing tiny, submicrometer-sized gold particles dispersed in water or another solvent[36].Michael Faraday published the first scientific paper on making gold nanoparticles in 1856, where he explained how he produced colloidal gold by reducing aurochloric acid ($HAuCl_4$) with phosphorus[34]. The method works on the idea that when a solution of HAuCl4 containing gold particles is quickly stirred with a reducing agent, it produces small, neutral gold atoms that are all about the same tiny size, smaller than a nanometer. This uniform size comes from the rapid mixing and chemical reaction taking place together [37,34]

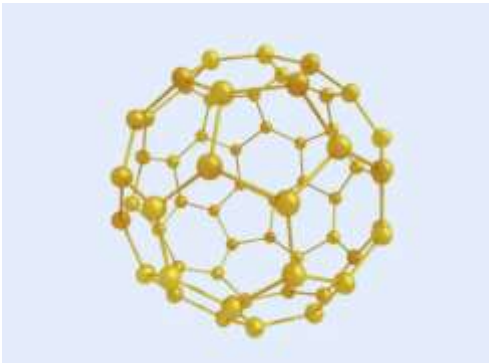


Fig No 6 : Gold Nanoparticles

Nanotechnology Future

Emerging innovations in advanced treatments and new drug delivery strategies have introduced a new era in targeted chemotherapy. Recently, the application of targeted nanoparticles has contributed to reducing both the incidence and mortality rates associated with breast cancer. However, several limitations and challenges still exist in integrating nanoparticles into medical practice. Future developments are expected to lower synthesis costs and improve pharmacokinetic properties, thereby enhancing the effectiveness of nanoparticles and addressing current constraints. Overall, numerous studies have shown that encapsulating anticancer drugs in

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nanoparticles significantly increases their therapeutic index in solid breast tumors. Nanotechnology thus holds great promise for improving both the diagnosis and treatment of cancer.

CONCLUSION

Nanotechnology in breast cancer treatment shows great promise by enhancing targeted drug delivery, reducing side effects, overcoming chemotherapy resistance, and improving therapeutic efficacy, particularly for aggressive types like triple-negative breast cancer (TNBC). Nanocarriers such as liposomes, niosomes, and nanoparticles enable precise delivery of drugs to tumor cells while sparing healthy tissue, leading to better patient outcomes with fewer adverse effects. This innovative approach is rapidly advancing, with ongoing research and clinical trials highlighting its potential to revolutionize breast cancer care.

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