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Review Article: "Review On Application Of Nanotechnology In Breast Cancer"

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Abstract

After lung cancer, breast cancer is the most prevalent form of cancer in women globally and one of the leading causes of death. Chemotherapy or radiation therapy combined with surgery are the treatment methods for breast cancer. The use of nanotechnology in cancer treatments has received a lot of attention lately. The physical and biological characteristics of nanoparticles in medicinal application are the focus of nanotechnology. In relation to traditional chemotherapeutic medications, TNPs offer a higher loading capacity, lower toxicity, and more stable drug delivery. Breast cancer diagnosis, therapy, and prevention are just a few of the many uses for nanotechnology. The use of traditional treatment approaches for breast cancer leads to problems and numerous negative effects. A more focused strategy for treating breast cancer is provided by nanotechnology. By directing medications to tumors, producing high concentrations, releasing pharmaceuticals gradually, improving drug stability, and minimizing side effects, nanoparticles enhance chemotherapy. An overview of breast cancer, its existing treatment options, and the current application of nanotechnology in breast cancer treatment are all included in this paper.

Keywords: breast cancer; chemotherapy; nanoparticles; nanotechnology; tumor.

Introduction

Cancer is a leading cause of death worldwide. Cancer is caused by a breakdown in the balance between cell growth and cell death, which leads to the creation of abnormal cells. This imbalanced disease is caused by gene deletion, mutation, and translocation, which results in genetic variance. Breast cancer is caused by abnormal cells growth in breast tissues, which results in lobular carcinoma (lobule cancer) and ductal carcinoma (ductal cancer). Both might be invasive or non-invasive. Mutations in genes such as BRCA1, BRCA2, RB, PIK3 and HER2, cause breast cancer to grow (1-4).

Breast cancer is the most frequent type of cancer after lung cancer, and it lead to women's cancer death in more than 100 nations. Reproductive, menstrual, and hormonal factors, family history, obesity, a high caloric diet, a lack of breastfeeding, the use of oral contraceptive pills, and the consumption of hormones such as estrogen in hormone replacement therapy are all potential risk factors for breast cancer. The most of deaths from breast cancer are caused by the disease's ability to metastasize to other organs. Breast cancer modulation and progression to metastasis include a number of pathways. There has been progress in understanding the biological activity of estrogen receptors (ERs), progesterone receptors (PRs), and human epidermal growth factor receptor 2 (HER2) in breast cancer subtypes. Chemotherapy, radiation, and surgery are the conventional methods of treating breast cancer. All of those have restrictions and several adverse effects. Chemotherapy is the application of nonspecific, cytotoxic anticancer medicines. They target both cancer cells and healthy cells in the body. Radiotherapy can also cause tissue damage around the cancer site. In addition, it affects the immunological system and causes fatigue, anemia, diarrhea, and

vomiting. The presence of breast cancer gene variations influences the utilization of radiation therapy as well. Individuals with pathogenic TP53 mutations are at a higher risk of developing new malignancies after radiation therapy. Additionally, chemotherapy and radiation therapy may raise the risk of heart disease. Surgery can be used to remove localized cancer, but it cannot treat metastatic cancer.

Nanotechnology refers to the scientific field that deals with the creation, manipulation and utilization of engineered manmade functional particles in nanoscale dimension (1-1000 nm range in at least one dimension), and applies them at atomic or molecular levels. As a result, nanomaterials allow for unique molecular interactions with biological systems, resulting in the development of 'Nano-oncology' applications such as tumor biomarker detection and profiling, in vivo tumor diagnostic imaging, and the delivery of more tailored medicines. However, Nano therapy, addresses all of the aforementioned issues by delivering targeted drugs to cancer cells with low toxicity, improved imaging, monitoring, and successful drug delivery. Nanoparticle's unique physiochemical features make them useful in the detection and treatment of a variety of disorders, particularly cancer. Chemotherapeutic medicines are encapsulated in nanoscale devices to improve the targeted delivery and bioavailability of breast cancer treatments. Nanomaterials are drug carriers that can be imaged, tracked, and targeted. According to study, the use of inorganic and organic nanoparticles can enhance the drawbacks of conventional therapies. Nanoparticles are a type of nanomedicine used to treat cancer. Nanoparticles are defined as particles with a size from 1 to 100 nm. Essentially, targeted drug delivery to the tumor location is facilitated by nanoparticles. Remote locations at the cancer site are better reached by nanoparticles. There are many different kinds of drug carriers, including micelles, polymeric dendrimers, microspheres, quantum dots (QDs), nanoemulsions, liposomes, hydrogels, and gold nanoparticles (GNPs). These carriers use a variety of drug attachment techniques, including encapsulation, adsorption, and covalent binding. Breast cancer can be diagnosed and treated by actively or passively delivering nanoparticles containing anticancer medicines to the targeted tumor (5-7).

Breast Cancer

According to WHO, malignant neoplasms represent a global burden for women. Breast cancer affects 19.6 million of the total 107.8 million life years adjusted for disability. Breast cancer is among the most often diagnosed cancers in women. Breast cancer incidence and mortality rates have increased during the last three decades. Breast cancer is projected to rise in the future as a result of westernized lifestyles such as delayed pregnancies, early menarche, a lack of physical activity, less nursing, and a bad diet(8). Cancer rates and death trends in the UK have been compared over 25 years, with a focus on the 35-69 year age group. This age group has better diagnostic accuracy and is more likely to experience future patterns of cancer. The data from 1993 to 2018 reveals that cancer trends in this age group reflect causal factors in the medium term past, rather than the longer term (9).

Breast cancer accounts for over one-third of all female cancers, making it the most prevalent disease among women. It is the primary cause of death and the second-leading cause of cancer mortality, after lung cancer. For female Americans in the 40–55 age range. One a woman's lifetime risk of unwanted breast cancer is 12.6%. Two out of every eight American women will have breast cancer at some time in their lives (10). The Breast and Cervical Cancer Mortality Prevention Act of 1990 authorized the CDC to establish comprehensive cancer screening programs through state health departments. The National Breast and Cervical Cancer Early Detection Program (NBCCEDP) was the first nationwide opportunity for states to build a public health infrastructure for cancer control. State health departments receive federal funding to provide cervical and breast cancer screening tests, diagnostic evaluations, and treatment referrals to lowincome, uninsured women. Guidelines for managing and evaluating common breast problems were developed by the CDC and general surgeons (11). Breast cancer is the most frequent malignancy in the US, with an estimated 313,510 diagnoses and 42,780 deaths in 2021. The Clinical Practice Guidelines for Oncology by the NCCN provide guidelines for managing patients with various types of cancer, including invasive and no metastatic. These guidelines are updated by a multidisciplinary panel of experts (12). Among other factors, the degree of disease progression determines the kind of treatment and how it is administered. The ladies are treated using a multiple types of techniques, which are referred to as combination treatment and include both surgical and systemic therapy. Currently, the primary approach to treating breast cancer is still surgery, which includes either mastectomy or breast conserving surgery. The rebuilding of the breast may be done concurrently with the amputation, postponed, or in conjunction with the dissection of the axillary lymph nodes (13,14).

Risk factors of breast cancer:

Non-modifiable factors: female sex, older age, family history, genetic mutations, pregnancy and breastfeeding.

Modifiable factors: hormonal replacement therapy, obesity, physical activity, alcohol intake, smoking.

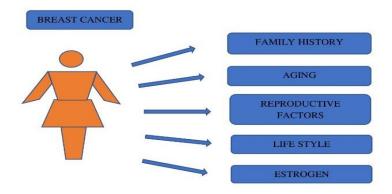


Fig. Risk Factors of Breast Cancer (15).

Breast cancer is primarily caused by inherited mutations in genes, including BRCA1 and BRCA2. Family history plays a significant role in the pathophysiology of the disease. Five to ten percent of total cases of breast cancer are caused by mutations in gene expression. Other known factors include obesity, hormone therapy, alcohol use, and over-expression of leptin in adipose tissue. Treatments include radiation therapy, surgery and chemotherapy, with new hope in treatment including adjuvant therapy, neoadjuvant therapy, and the introduction of mono-clonal antibodies and enzyme inhibitors. Mutations in the PI3K/AKT pathway and RAS/MEK/ERK pathway can lead to uncontrolled proliferation of tumor cells. Overexpression of leptin in breast adipose tissues is also responsible for breast cancer (16).

Classification

Histological classification

The morphological analysis of breast cancer involves determining if the tumor is only affect the epithelial component or invaded the surrounding stroma. Histopathological practice considers features of the cell type, quantity of cells, secretion type, immunohistochemical profile, and architectural characteristics. IDCs, which are about 50% to 80% of newly diagnosed cases, can be classified as "no specific type" or "special type" based on their distinctive characteristics and molecular behaviour (17–21).

Molecular classification

Breast cancer is a diverse disease with varying clinical and treatment responses (22). Modern medicine focuses on analyzing molecular patterns to group tumors into classes or entities, aiding in clinical management, epidemiological studies, and clinical trials, as only morphological classification and pathological parameters can predict tumor pathophysiology (23). There were four molecular subgroups shown to be clinically significant: Luminal A and B, Triple Negative and enriched HER2 (HER2+). These subtypes are mainly influenced by genes related to estrogen receptors, progesterone receptors, HER2, and cell proliferation regulator. Immunohistochemical panels have been effective in stratifying these molecular entities. Multigenic assays like Oncotype DX, Prosigna PAM50, and Mammaprint have been developed to improve risk stratification and prognosis determination (24–26).

Luminal Breast Cancer

Luminal breast cancers are estrogen receptor (ER) positive. The most frequent molecular subtype of breast cancer, comprising half of newly diagnosed cases, has a high immunohistochemical profile with ER+, PR, HER2-, and Ki-67 levels. These tumors have luminal epithelial cell characteristics and include low histological grade variants. They have a favorable prognosis and less lymph node involvement (27–29). Luminal B breast cancer is responsible for 20%-30% of invasive cases and can be classified into Luminal B (HER-) and Luminal B (HER2+). The subtype is aggressive and often requires additional treatments like chemotherapy or targeted target therapy. It is associated with a moderate histological grade and an intermediate prognosis. The primary difference between the two luminous subgroups is the increased expression of genes related to cell proliferation and the activation of alternative growth factor pathways. Compared to luminal A cancers, luminal B tumors have a worse prognosis, low expression of ER-related genes, variable expression of HER2neu-related genes, and high expression of proliferation-related genes. Instead of using traditional molecular diagnostics, the St. Gallen International Expert Consensus on the "Primary Therapy of Early Breast Cancer 2013" suggested that immunohistochemistry for ERs, PRs, HER2neu, and ki67 index be used to define luminal subtypes of breast cancer. The Ki67 index is used to categorize luminal cancers since it shows the percentage of proliferative genes and cells. Because endocrine therapy or chemotherapy alone may not be sufficient in certain situations, the Ki67 index is frequently used to customize the patient's treatment (30–32).

Breast Cancer Types

HER2 Positive Breast Cancer

HER2 positive and ERs and PRs negative are its defining characteristics. Instead of basal and luminal genes and proteins, this subtype expresses genes and proteins linked to proliferation. HER2 positive individuals are varied and possess both basal and luminal characteristics, bridging the gap between the two. These malignancies have the worst prognosis and proliferate more quickly than luminal cancers. When it comes to cell migration, this subtype's cells are more aggressive than the luminal cells. 15% to 25% of invasive breast cancers have tumors with HER2 overexpression, which have a poorer prognosis but react favorably to HER2-targeted treatments. Within HER2-positive tumors, there are diverse intrinsic subtypes, suggesting the possibility of forecasting the extent of a patient's reaction to trastuzumab. In the 4-year follow-up to the National Surgical Adjuvant Breast and Bowel Project B-31 trials, hormone receptor positive tumors were linked to higher disease-free survival and overall survival compared to hormone receptor negative tumors within the HER2 subtype of breast cancer, regardless of clinicopathologic factors (33). According to the NCCN centers' initial 5-year follow-up results, women with HR-negative/HER2positive tumors had a higher PCR rate than those with HR-positive/HER2-positive tumors, and they reported more cancer recurrences from the HR-negative tumor group than the HR-positive tumor group. Women with HR-negative/HER2-positive tumors also showed fewer first recurrences in bone and more recurrences in the brain (34). Trastuzumab, an anti-HER2 agent, significantly enhanced prognosis for those with breast cancer that is HER2-positive. Lapatinib, an oral tyrosine kinase inhibitor, was added to the standard of care for advanced HER2-positive illness due to its enhancement in progression-free survival when combined with capecitabine. Pertuzumab, a humanized monoclonal antibody, binds to HER2 on extracellular domain II, blocking HER2/HER3 and activating intracellular signalling cascades, including cell proliferation and survival. However, no improvement in overall survival was observed in a phase III trial (35-38).

Triple-Negative Breast Cancer

Triple-negative breast cancers (TNBCs) are aggressive types of breast cancer caused by impaired expression of estrogen and progesterone receptors and human growth factor receptor 2. TNBCs are defined by human growth factor receptor 2 expressions ranging from 0 to 1+ and cellular expression of these receptors of ≤1%. TNBCs can be categorized into six subgroups based on molecular heterogeneity: luminal androgen receptor expression, immunomodulatory, mesenchymal-like, mesenchymal stem-like, basal-like, and unstable. They are spontaneously recurring and account for 12−17% of all breast cancers. TNBCs represent 24% of newly diagnosed breast cancers and have a steady increase in incidence. In 2018, 2,088,849 cases were reported, making it a common cancer in women. The average survival rate from

TNBC is approximately 10.2 months, with a 65% 5-year survival rate in regional tumors and 11% in those expanded to distant organs (39–43).

Treatment for Breast Cancer

Surgery There are two major types of surgical procedures for removal of breast cancerous tissue are breast conserving surgery and mastectomy. Breast conserving therapy (BCT) involves excision of tumor (lumpectomy). Physical examination, diagnostic ultrasound and mammography are imaging modalities use to choose patients for BCT. Young age, aggressive tumor subtype (HER2 positive and triple negative) are not suitable for BCT. Mastectomy is a complete removal of breast. There are three categories of mastectomy available to patients: skin-sparing mastectomy, nipple areolar mastectomy and total mastectomy (44,45).

Chemotherapy Chemotherapy is a systemic treatment for breast cancer, ranging from neoadjuvant to adjuvant. It is individualized based on the tumor's characteristics and can be used in secondary breast cancer. Neoadjuvant chemotherapy is used for advanced, inflammatory breast cancers, downstaging large tumors, or small tumors with worse prognostic molecular subtypes. Treatment includes a simultaneous application of drugs like carboplatin, cyclophosphamide, 5-fluorouracil/capecitabine, taxanes, and anthracyclines. The choice of the right drug is crucial as different molecular breast cancer subtypes react differently to chemotherapy before surgery. However, chemotherapy often leads to side effects like nausea, hair loss, diarrhea, mouth sores, fatigue, increased susceptibility to infections, bone marrow supression, leucopenia, anemia, easier bruising or bleeding, cardiomyopathy, neuropathy, hand-foot syndrome, impaired mental functions, and disruptions of the menstrual cycle and fertility issues in younger women (46).

Radiation Therapy Radiotherapy is a local treatment for breast cancer, typically provided after surgery or chemotherapy. It aims to destroy cancerous cells and minimize recurrence. Common techniques include breast radiotherapy, chest-wall radiotherapy, and breast boost. There are several types of breast radiotherapy, including intraoperative, 3D-conformal, intensity-modulated, and brachytherapy. Despite common side effects like fatigue and skin irritation, radiation therapy improves overall survival rates and reduces recurrence risk (47).

Endocrinal (Hormonal) Therapy Endocrinal therapy is used as a neoadjuvant or adjuvant in patients with Luminal-molecular subtype of breast cancer, particularly in cases of recurrence or metastasis. It aims to lower estrogen levels or prevent breast cancer cells from being stimulated by estrogen. Drugs like selective estrogen receptor modulators and aromatase inhibitors block ERs, while ovarian suppression and chemotherapy drugs also help. However, approximately 50% of hormoneoreceptor-positive breast cancer become resistant (48–50).

Limitations to Conventional Therapy

Chemotherapy is a common treatment for most cancers, including breast cancer, which often includes biological medicines that have additive or synergistic effects. Chemotherapy destroys neoplastic cells due to their fast division, damaging healthy cells like bone marrow, macrophages, digestive tract, and hair follicles. However, conventional chemotherapy cannot provide targeted action on cancer cells, leading to side effects like myelosuppression, mucositis, alopecia, organ dysfunction, and anemia or thrombocytopenia. Chemotherapeutic drugs are often absorbed by macrophages and removed from the bloodstream, making them useless. Additionally, low solubility of medications and the overexpression of P-glycoprotein, a multidrug resistance protein, prevent drug accumulation inside tumors and mediate drug resistance. While chemotherapy and adjuvant therapies have proven efficacious, side effects can be serious and even life-threatening. To enhance the therapeutic index and efficacy/toxicity balance for advanced breast cancer, a unique therapy approach involving selective delivery of cytotoxic drugs to tumor masses is needed (51,52)

Nanotechnology in Breast Cancer

Selective cancer targeting has seen a significant transformation thanks to nanotechnology. "The creation of useful materials, devices, and systems used to manipulate matter that are small scale ranging between 1 and 100 nm" was the initial definition of nanotechnology. Nanoparticles can be modified in a variety of ways, including shape, size, and chemical characteristics, in order to target certain cells. They can use either active or passive targeting to target the cancerous cells. Many different types of nano-delivery systems with different materials and physiochemical properties have been developed for application to various diseases. Most well studied among these are liposomes, dendrimers, gold nanoshells, nanocrystal, carbon-60 fullerenes, silicon- and silica-based nanoparticle, and super paramagnetic nanoparticulates. An excellent example of nanotechnology achieved in the field of medicine is liposomal drug delivery. Various liposomal doxorubicin formulations have been successfully used in the clinic to treat the breast cancer. The three primary parts of a targeted delivery system based on nanotechnology are (i) an anticancer medication that induces apoptosis, (ii) a targeting moiety penetration booster, and (iii) a carrier (53,54).

Active Targeting: When active targeting is used, chemotherapeutic drugs are encapsulated in nanoparticles that are engineered to engage directly with the damaged cells. Active targeting is based on molecular recognition. In order to target the malignant cells, the nanoparticles surface is altered. For molecular recognition, targeted chemicals are often affixed to the surface of nanoparticles. Through either ligand-receptor interaction or antibody-antigen recognition, the designed nanoparticles target cancerous cells. A nanoparticle is made of a number of materials. Metals, lipids, ceramics, and polymers are often utilized materials. At the molecular level, cancerous cells are different from healthy cells due to certain special characteristics. Their distinctive characteristic is the overexpression of certain receptors on their surface. Nanoparticles can only target malignant cells because of the complimentary ligands that are attached to their surface. Following their binding to the receptors, the nanoparticles quickly undergo receptor-mediated endocytosis or phagocytosis by cells, which causes the drug to be internalized by the cells (55).

Passive Targeting: Nanoparticles can also target cancer through passive targeting. Cancerous cells continue to improperly absorb nutrients through the blood vessels, creating large, leaky blood vessels surrounding the cells while apoptosis is halted. Abnormalities in the basement membrane and a decrease in the number of pericytes lining rapidly growing endothelial cells result in the formation of leaky blood vessels. As a result, chemicals have a higher permeability to penetrate the vessel wall enclosing tumor cells. The holes of leaky endothelial cells range in size from 100 to 780 nm (56). As a result, nanoparticles smaller than that can easily pass through the holes. In order to concentrate the medication within a certain organ and penetrate the tumor cells by passive diffusion or convection, nanoparticles can be directed to a specific region of the capillary endothelium. The diffusion mechanism is facilitated by a lack of lymphatic drainage. A gel-like fluid and a network of collagen make up the tumor interstitium. The fluid's high interstitial pressures prevent molecules from flowing inward. Additionally, tumors have leaky vascular and poorly defined lymphatic networks. As a result, medications that penetrate the interstitial space may have long retention periods in the interstitium of tumors. The increased permeability and retention effect is the name given to this characteristic. Through improved permeability and retention, nanoparticles can readily accumulate selectively before diffusing into the cells (57,58).

Active and Passive Targeting by Nanoparticles Targeting Agents:

Nanocarriers, which include anticancer medications, targeting moieties, and polymers, are employed as targeting agents in cancer therapy. Liposomes, dendrimers, micelles, carbon nanotubes, nanocapsules, nanospheres, and many more are examples of the various types of nanocarriers. The nanoparticles can be adsorbed, encapsulated, covalently bonded, or entrapped with therapeutic substances. Lipid bilayers make up **liposomes**, and the amount of lipid bilayers determines whether the core is hydrophilic or hydrophobic. While liposomes with several lipid bilayers entrap lipid-soluble pharmaceuticals, those with a single lipid bilayer contain an aqueous core for encapsulating water-soluble medications. For stabilization under physiological settings, they are coated with inert polymers and easily removed by macrophages. Polyethylene glycol is frequently used to coat liposomes. For targeted medication delivery, liposomal nanoparticles can combine with ligands or antibodies (59,60).

Dendrimers are multipurpose structures that resemble branched three-dimensional trees. They are made from natural or manufactured materials like sugars, nucleotides, and amino acids. By carefully polymerizing the monomers, dendrimers can be created while retaining the appropriate size and form (61). Dendrimers are highly branched macromolecules controlled in size and shape. They can be fabricated using convergent or divergent step growth polymerization. Dendrimers are attractive drug carrier candidates due to their well-defined structure, monodispersity of size, surface functionalization capability, and stability. They are being investigated for drug and gene delivery, penicillin carriers, and anticancer therapy. Dendrimers typically include polymers like polyamidoamine, melamine, poly L-glutamic acid, polyethyleneimine, polyethylene glycol (62). Micelle nanoparticles with a core-shell structure are formed by amphiphilic copolymers, with a hydrophilic shell and a hydrophobic drug reservoir. These micelles inhibit protein adsorption, improving drug solubility. Pluronic block copolymers, composed of poly(propylene oxide) and poly(ethylene oxide), are widely used in drug delivery systems and are believed to associate with energy metabolism in Multidrug Resistance cancer cells (63). The spherical **nanospheres** are made of a matrix system that distributes the drug uniformly through encapsulation, adhesion, or entrapment. For targeting reasons, ligands or antibodies can be added to these nanoparticles' surface to alter it. A polymeric membrane encloses the central core of **nanocapsules**, which resemble vesicles and contain a medication. Targeting ligands or antibodies can be linked to the surface (64,65). The class of compounds known as **fullerenes** and **nanotubes** is composed of carbon atoms shaped like hollow spheres or ellipsoid tubes. Fullerenes have the potential to trap atoms while binding ligands or antibodies to their surface for targeting. Since carbon nanotubes can be attached to a wide range of active molecules, including proteins, peptides, nucleic acids, and medicinal substances, they are altered to become functionalized and water soluble. Both single and multi-walled nanotubes are possible (66). Gold nanoparticles optical characteristics, biocompatibility, inertness, and ease of fabrication have led to extensive research into them as photothermal agents and drug carriers. GNPs have the potential to be used as photothermal therapy agents for the treatment of cancer because to their surface plasmon resonance properties. The electronphonon and phonon-phonon interactions in gold nanoparticles allow them to produce heat when light is absorbed. Using antibody-conjugated nanoparticles exposed to shorter laser pulses, for example, localized cell injury was shown (67,68). **Quantum dots** are semiconductor-like inorganic nanocrystals with a diameter of 1-10 nm. Synthesized from elements in groups II-VI or III-V of the periodic table, QDs consist of CdSe nanoparticles and ZnS shell. They have a large medication loading capacity and are useful in biological imaging, cancer diagnosis, and therapeutic operations. QDs are photo stable for extended periods, making them ideal for breast cancer research (69).

Conclusion

Since cancer is one of the most deadly illnesses, nanotechnology can help with precision treatment while preventing potentially fatal side effects. One of the rapidly expanding areas of medical science is nanotechnology. Nanotechnology is drastically altering the course of treatment and has already transformed cancer therapy in numerous ways. It has significantly improved the ability to identify malignant cells specifically, administer drugs precisely, and get around the drawbacks of traditional chemotherapies. Treatment techniques have greatly advanced thanks to nanotechnology. Compared to traditional particles, nanoparticles have advantages. From coupling with anti-breast cancer antibodies to surface changes for improved drug delivery, nanomaterials provide a wide range of functionalization choices.

Even if a number of procedures have been created, additional research is necessary to completely grasp the nanomaterial's potential and capabilities to advance therapeutic methods. These innovative active or passive targeting techniques can significantly improve the survival rate by reducing the negative effects of conventional chemotherapies. Making the delivery systems much smaller than their intended size is necessary for precise drug release into extremely specific targets. It is strongly anticipated that the developments in nanotechnology would enable the realization of these tiny medication delivery systems. An overview of every facet of medication delivery with nanocarriers to treat the breast cancer is given in this article. Numerous formulations based on nanotechnology are now undergoing research and clinical studies, while some have already been introduced to the market. Due to toxicity issues, there are currently few clinical trials on the use of nanomaterials in the treatment of breast cancer; nonetheless, numerous studies have indicated that the future of nanomedicine in this field appears to be promising. The significance of nanotechnology to the treat the breast and other cancers in the future has been acknowledged by the National Cancer Institute, which has awarded significant grants to further this research.

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References

- 1. Dai X, Cheng H, Bai Z, Li J. Breast cancer cell line classification and Its relevance with breast tumor subtyping. Vol. 8, Journal of Cancer. Ivyspring International Publisher; 2017. p. 3131–41.
- 2. Alshareeda AT, Nur Khatijah MZ, Al-Sowayan BS. Nanotechnology: A revolutionary approach to prevent breast cancer recurrence. Vol. 46, Asian Journal of Surgery. Elsevier (Singapore) Pte Ltd; 2023. p. 13-7.
- Tanaka T, Decuzzi P, Cristofanilli M, Sakamoto JH, Tasciotti E, Robertson FM, et al. Nanotechnology 3. for breast cancer therapy. Vol. 11, Biomedical Microdevices. 2009. p. 49-63.
- 4. Sutradhar KB, Amin MdL. Nanotechnology in Cancer Drug Delivery and Selective Targeting. ISRN Nanotechnology. 2014 Jan 16;2014:1–12.
- 5. Ganesan K, Wang Y, Gao F, Liu Q, Zhang C, Li P, et al. Targeting engineered nanoparticles for breast cancer therapy. Vol. 13, Pharmaceutics. MDPI; 2021.
- Tang X, Loc WS, Dong C, Matters GL, Butler PJ, Kester M, et al. The use of nanoparticulates to treat 6. breast cancer. Vol. 12, Nanomedicine. Future Medicine Ltd.; 2017. p. 2367–88.
- 7. Singh SK, Singh S, Wlillard J, Singh R. Drug delivery approaches for breast cancer. Vol. 12, International Journal of Nanomedicine. Dove Medical Press Ltd.; 2017. p. 6205–18.
- Łukasiewicz S, Czeczelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast cancer— 8. epidemiology, risk factors, classification, prognostic markers, and current treatment strategies— An updated review. Vol. 13, Cancers. MDPI; 2021.
- 9. Shelton J, Zotow E, Smith L, Johnson SA, Thomson CS, Ahmad A, et al. 25 year trends in cancer incidence and mortality among adults aged 35-69 years in the UK, 1993-2018: retrospective secondary analysis. BMJ. 2024;
- 10. Richie RC, Swanson JO. Breast Cancer: A Review of the Literature. Vol. 35, Journal of Insurance Medicine J Insur Med. 2003.
- 11. Cady B, Steele GD, Morrow M, Gardner B, Smith BL, Lee NC, et al. Evaluation of common breast problems: guidance for primary care providers. CA Cancer J Clin. 1998 Jan 1;48(1):49–63.
- 12. Gradishar WJ, Moran MS, Abraham J, Abramson V, Aft R, Agnese D, et al. Breast Cancer, Version 3.2024. JNCCN Journal of the National Comprehensive Cancer Network. 2024 Jul 1;22(5):331-57.
- 13. Cipora E, Konieczny M, Karwat ID, Roczniak W, Babuśka-Roczniak M. Surgical method of treatment and level of satisfaction with life among women diagnosed with breast cancer, according to time elapsed since performance of surgery. Annals of Agricultural and Environmental Medicine. 2018;25(3):453-9.
- Murawa P, Murawa D, Adamczyk B, Połom K. Breast cancer: Actual methods of treatment and 14. future trends. Vol. 19, Reports of Practical Oncology and Radiotherapy. Urban and Partner; 2014. p. 165-72.

- 15. Sun YS, Zhao Z, Yang ZN, Xu F, Lu HJ, Zhu ZY, et al. Risk factors and preventions of breast cancer. Vol. 13, International Journal of Biological Sciences. Ivyspring International Publisher; 2017. p. 1387–97.
- 16. Majeed W, Aslam B, Javed I, Khaliq T, Muhammad F, Ali A, et al. Breast cancer: Major risk factors and recent developments in treatment. Asian Pacific Journal of Cancer Prevention. 2014;15(8):3353–8.
- 17. Nascimento RG do, Otoni KM. Histological and molecular classification of breast cancer: what do we know? Mastology. 2020;30.
- 18. Makki J. Diversity of breast carcinoma: Histological subtypes and clinical relevance. Clin Med Insights Pathol. 2015;8(1):23–31.
- 19. Henry NL, Cannon-Albright LA. Breast cancer histologic subtypes show excess familial clustering. Cancer. 2019 Sep 15;125(18):3131–8.
- 20. Nounou MI, Elamrawy F, Ahmed N, Abdelraouf K, Goda S, Syed-Sha-Qhattal H. Breast cancer: Conventional diagnosis and treatment modalities and recent patents and technologies supplementary issue: Targeted therapies in breast cancer treatment. Breast Cancer (Auckl). 2015 Sep 27;9:17–34.
- 21. Masood S. Breast cancer subtypes: Morphologic and biologic characterization. Women's Health. 2016 Jan 1;12(1):103–19.
- 22. Feng Y, Spezia M, Huang S, Yuan C, Zeng Z, Zhang L, et al. Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis. Vol. 5, Genes and Diseases. Chongqing University; 2018. p. 77–106.
- 23. Fragomeni SM, Sciallis A, Jeruss JS. Molecular Subtypes and Local-Regional Control of Breast Cancer. Vol. 27, Surgical Oncology Clinics of North America. W.B. Saunders; 2018. p. 95–120.
- 24. Bernard PS, Parker JS, Mullins M, Cheung MCU, Leung S, Voduc D, et al. Supervised risk predictor of breast cancer based on intrinsic subtypes. Journal of Clinical Oncology. 2009 Mar 10;27(8):1160–7.
- 25. Paik S, Shak S, Kim C, Baker J, Cronin M, Baehner FL, et al. Division of Pathology, NSABP, 4 Allegheny Center [Internet]. Vol. 27, n engl j med. 2004. Available from: www.nejm.org
- 26. Arc M, Van De V Ijver J, Udong Y, Van 'T V Eer AJ, Ongyue H, Ai D, et al. The New England Journal of Medicine A GENE-EXPRESSION SIGNATURE AS A PREDICTOR OF SURVIVAL IN BREAST CANCER A BSTRACT Background A more accurate means of prognos [Internet]. Vol. 347, N Engl J Med. 2002. Available from: www.nejm.org
- 27. Goldhirsch A, Winer EP, Coates AS, Gelber RD, Piccart-Gebhart M, Thürlimann B, et al. Personalizing the treatment of women with early breast cancer: Highlights of the st gallen international expert consensus on the primary therapy of early breast Cancer 2013. Annals of Oncology. 2013 Sep 1;24(9):2206–23.
- 28. Hashmi AA, Aijaz S, Khan SM, Mahboob R, Irfan M, Zafar NI, et al. Prognostic parameters of luminal A and luminal B intrinsic breast cancer subtypes of Pakistani patients. World J Surg Oncol. 2018 Jan 2;16(1).
- 29. Gao JJ, Swain SM. Luminal A Breast Cancer and Molecular Assays: A Review. Oncologist. 2018 May 1;23(5):556–65.

- 30. Fan C, Oh DS, Wessels L, Weigelt B, Nuyten DSA, Nobel AB, et al. Concordance among Gene-Expression-Based Predictors for Breast Cancer A bs tr ac t [Internet]. 2006. Available from: www.nejm.org
- 31. Hu Z, Fan C, Oh DS, Marron JS, He X, Qaqish BF, et al. The molecular portraits of breast tumors are conserved across microarray platforms. BMC Genomics. 2006 Apr 27;7.
- 32. Janardhan A, Kumar AP, Viswanath B, Saigopal DVR, Narasimha G. Production of Bioactive Compounds by Actinomycetes and Their Antioxidant Properties. Biotechnol Res Int. 2014 Mar 26;2014:1–8.
- 33. Perez EA, Romond EH, Suman VJ, Jeong JH, Sledge G, Geyer CE, et al. Trastuzumab plus adjuvant chemotherapy for human epidermal growth factor receptor 2 Positive breast cancer: Planned joint analysis of overall survival from NSABP B-31 and NCCTG N9831. Journal of Clinical Oncology. 2014 Nov 20;32(33):3744–52.
- 34. Vaz-Luis I, Ottesen RA, Hughes ME, Marcom PK, Moy B, Rugo HS, et al. Impact of hormone receptor status on patterns of recurrence and clinical outcomes among patients with human epidermal growth factor-2-positive breast cancer in the National Comprehensive Cancer Network: a prospective cohort study. Breast Cancer Research. 2012 Oct 1;14(5).
- 35. Slamon DJ, Clark GM, Wong SG, Levin WJ, Ullrich A, McGuire WL. Human breast cancer: Correlation of relapse and survival with amplification of the HER-2/neu oncogene. Science (1979). 1987;235(4785):182–91.
- 36. Ennis S Lamon DJ, Rian Eyland -j Ones BL, Teven Hak SS, Ank Uchs HF, Irginia Aton VP, Harm PD, et al. The New England Journal of Medicine USE OF CHEMOTHERAPY PLUS A MONOCLONAL ANTIBODY AGAINST HER2 FOR METASTATIC BREAST CANCER THAT OVEREXPRESSES HER2 Background The HER2 gene, which encodes the [Internet]. Vol. 344, N Engl J Med. 2001. Available from: www.nejm.org
- 37. Geyer CE, Forster J, Lindquist D, Chan S, Gilles Romieu C, Pienkowski T, et al. Lapatinib plus Capecitabine for HER2-Positive Advanced Breast Cancer A bs t r ac t [Internet]. 2006. Available from: www.nejm.org
- 38. Lewis Phillips GD, Li G, Dugger DL, Crocker LM, Parsons KL, Mai E, et al. Targeting HER2-positive breast cancer with trastuzumab-DM1, an antibody-cytotoxic drug conjugate. Cancer Res. 2008 Nov 15;68(22):9280–90.
- 39. Medina MA, Oza G, Sharma A, Arriaga LG, Hernández JMH, Rotello VM, et al. Triple-negative breast cancer: A review of conventional and advanced therapeutic strategies. Vol. 17, International Journal of Environmental Research and Public Health. MDPI AG; 2020.
- 40. Ghoncheh M, Pournamdar Z, Salehiniya H. Incidence and mortality and epidemiology of breast cancer in the world. Asian Pacific Journal of Cancer Prevention. 2016;17:43–6.
- 41. Suleman M, Tahir ul Qamar M, Saleem S, Ahmad S, Ali SS, Khan H, et al. Mutational Landscape of Pirin and Elucidation of the Impact of Most Detrimental Missense Variants That Accelerate the Breast Cancer Pathways: A Computational Modelling Study. Front Mol Biosci. 2021 Jun 28;8.
- 42. Singh S, Numan A, Agrawal N, Tambuwala MM, Singh V, Kesharwani P. Role of immune checkpoint inhibitors in the revolutionization of advanced melanoma care. Vol. 83, International Immunopharmacology. Elsevier B.V.; 2020.
- 43. Almansour NM. Triple-Negative Breast Cancer: A Brief Review About Epidemiology, Risk Factors, Signaling Pathways, Treatment and Role of Artificial Intelligence. Vol. 9, Frontiers in Molecular Biosciences. Frontiers Media S.A.; 2022.

- 44. Rahman GA. Editorial: Breast conserving therapy: A surgical technique where little can mean more. Vol. 3, Journal of Surgical Technique and Case Report. 2011. p. 1–4.
- 45. Cardoso F, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rubio IT, et al. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology. 2019 Aug 1;30(8):1194–220.
- 46. Rouzier R, Perou CM, Symmans WF, Ibrahim N, Cristofanilli M, Anderson K, et al. Breast cancer molecular subtypes respond differently to preoperative chemotherapy. Clinical Cancer Research. 2005 Aug 15;11(16):5678–85.
- 47. Chandra Joshi S, Khan FA, Pant I, Shukla A. Role of Radiotherapy in Early ... Role of Radiotherapy in Early Breast Cancer: An Overview. Vol. 1, International Journal of Health Sciences. 2007.
- 48. Tremont A, Lu J, Cole JT. Endocrine Therapy for Early Breast Cancer: Updated Review.
- 49. Jones KL, Buzdar AU. A review of adjuvant hormonal therapy in breast cancer. Vol. 11, Endocrine-Related Cancer. 2004. p. 391–406.
- 50. Drăgănescu M, Carmocan C. Hormone therapy in breast cancer. Vol. 112, Chirurgia (Romania). Editura Celsius; 2017. p. 413–7.
- 51. Nguyen KT. Targeted nanoparticles for cancer therapy:Promises and challenges. Vol. 2, Journal of Nanomedicine and Nanotechnology. 2011.
- 52. Zhao G, Leticia Rodri<mark>guez B. Molecular t</mark>arge<mark>ting of liposo</mark>mal nanoparticles to tumor microenvironment. Vol. 8, International Journal of Nanomedicine. 2012. p. 61–71.
- 53. Wang R, Billone PS, Mullett WM. Nanomedicine in action: An overview of cancer nanomedicine on the market and in clinical trials. Vol. 2013, Journal of Nanomaterials. 2013.
- 54. Praetorius N, Mandal T. Engineered Nanoparticles in Cancer Therapy. Recent Pat Drug Deliv Formul. 2008 May 14;1(1):37–51.
- 55. Cho K, Wang X, Nie S, Chen Z, Shin DM. Therapeutic nanoparticles for drug delivery in cancer. Vol. 14, Clinical Cancer Research. 2008. p. 1310–6.
- 56. Hobbs SK, Monsky WL, Yuan F, Gregory Roberts W, Griffith L, Torchilin VP, et al. Regulation of transport pathways in tumor vessels: Role of tumor type and microenvironment [Internet]. Vol. 95, Medical Sciences. 1998. Available from: www.pnas.org.
- 57. Au -S, Jang SH, Zheng J, Chen CT, Song S, Hu L, et al. Determinants of drug delivery and transport to solid tumors [Internet]. Vol. 74, Journal of Controlled Release. 2001. Available from: www.elsevier.com/locate/jconrel
- 58. Maeda * H, Wu J, Sawa T, Matsumura Y, Hori K. Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review a, a a b c [Internet]. Vol. 65, Journal of Controlled Release. 2000. Available from: www.elsevier.com/locate/jconrel
- 59. Salkho NM, Paul V, Kawak P, Vitor RF, Martins AM, Al Sayah M, et al. Ultrasonically controlled estrone-modified liposomes for estrogen-positive breast cancer therapy. Artif Cells Nanomed Biotechnol. 2018 Nov 5;46(sup2):462–72.
- 60. Guo C, Chen Y, Gao W, Chang A, Ye Y, Shen W, et al. Liposomal nanoparticles carrying anti-IL6R antibody to the tumour microenvironment inhibit metastasis in two molecular subtypes of breast cancer mouse models. Theranostics. 2017;7(3):775–88.
- 61. Diederich F, Atrice Felber B. Supramolecular chemistry of dendrimers with functional cores [Internet]. Vol. 16, PNAS April. 2002. Available from: www.pnas.orgcgidoi10.1073pnas.052568099

IJCR

- Hughes GA. Nanostructure-mediated drug delivery. Vol. 1, Nanomedicine: Nanotechnology, 62. Biology, and Medicine. 2005. p. 22-30.
- Yuan Y, Cai T, Xia X, Zhang R, Chiba P, Cai Y. Nanoparticle delivery of anticancer drugs overcomes 63. multidrug resistance in breast cancer. Vol. 23, Drug Delivery. Taylor and Francis Ltd; 2016. p. 3350-7.
- Brigger I, Dubernet C, Couvreur´ P, Couvreur´ C. N anoparticles in cancer therapy and diagnosis 64. Vol. 54, Advanced Drug Delivery Reviews. 2002. Available www.elsevier.com/locate/drugdeliv
- Anajwala CC, Jani GK, Vijayendra Swamy S. Current Trends of Nanotechnology for Cancer Therapy 65. 1043.
- 66. Yadav J. Fullerene: Properties, Synthesis and Application. 2017;1–6. Available from: www.stmjournals.com
- Wang F, Li C, Cheng J, Yuan Z. Recent advances on inorganic nanoparticle-based cancer therapeutic 67. agents. Vol. 13, International Journal of Environmental Research and Public Health. MDPI; 2016.
- 68. Pitsillides CM, Joe EK, Wei X, Rox Anderson R, Lin CP. Selective Cell Targeting with Light-Absorbing Microparticles and Nanoparticles. Vol. 84, Biophysical Journal. 2003.
- 69. David ME, Grigore ME. 3 Organic and Inorganic Nano-Systems Used in Cancer Treatment [Internet]. Vol. 1, J Med Res Health Educ. 2017. Available from: http://www.imedpub.com/medical-researchand-health-education/iMedPubJournalshttp://www.imedpub.com