Original Article

Recent Advancement of Nano Formulations in Treatment of Breast Cancer

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Abstract

Breast cancer is a major ongoing public health issue among women in both developing and developed countries. The most common kind of breast cancer is adenocarcinoma, which includes invasive carcinoma and ductal carcinoma in situ (DCIS). A doctor can determine the stage of cancer based on the size of the tumour and if it has spread to the lymph nodes or other parts of the body. Breast Cancer Etiology Women must get general health tests to detect risk factors connected to an increased incidence of breast cancer development. Breast cancer risk factors may be classified into seven primary categories. Breast cancer epidemiology includes Breast cancer is the second-leading cause of cancer-related deaths among women worldwide, and it affects women more frequently than any other kind of cancer. Breast cancer was discovered in around 2.3 million females in 2020 and 685 000 individuals died as a result of the disease. It is critical that varied populations place a high priority on breast cancer prevention and control strategies. Raising awareness of risk factors and early detection is very critical in developing countries. As a rapidly developing field, nanotechnology brings promising opportunities to human cancer diagnosis and treatment. The use of nanoparticulate based platforms overcomes biological barriers and allows prolonged blood circulation time, simultaneous tumor targeting and enhanced accumulation of drugs in tumors. In this article authors have focused on various approach in diagnosis of breast cancer, as well as recent advancement in treatment of same using nanoparticles approach.

Keywords: breast cancer, gene/drug delivery, nanoparticle, etiology, epidemiology, diagnosing, approaches, risk factors, nanotechnology.

INTRODUCTION

The most frequent cancer in women and the main cause of mortality is breast cancer. Breast cancer care is facing additional challenges brought on by metastasis and tumor recurrence [(1)]. Ducts connecting the lobes, lobules (milk-producing glands), and bulbs go to the nipple in the centre of the areola, a dark region of skin. Additionally, there are blood arteries in each breast that connect to lymphatic veins and the tiny bean-shaped lymph nodes. The axillary and internal mammary lymph nodes, which are found around the borders of the breast in the underarm, above the collarbone, and in the chest, are where the majority of the lymphatic veins run. The principal pathway of regional spread in the metastases of the initial breast cancer is frequently the axillary lymph nodes, which are found beneath the arm [(2)]. Women are more often than males being diagnosed with breast cancer; up to 7% of cases in women under 40 and fewer than 4% in those under 35 are diagnosed with the disease, respectively. In US and other developed nations, breast cancer affects more women than any other type of cancer. Nearly one in three cancer cases, or 61,000 new instances of in situ breast cancer and 249,000 new instances of aggressive breast cancer are expected to develop in the USA alone in 2016. According to WHO data, there will be 2.3 million women diagnosed with breast cancer and 685,000 deaths worldwide in 2020. By the year 2020, 7.8 million thriving females had had breast cancer in the prior five years, making it the most common disease in the globe [(3)]. A new breast bulge or swelling armpit, breast expansion or enlargement of the breast, irritation of the breast skin, redness or flaky skin in the nipple region, pulling in of the nipple or discomfort in the nipple area, nipple discharge other than breast milk, including blood, any change in the size or form of the breast, and soreness in any portion of the breast [(4)]. Radiation therapy, chemotherapy, hormone therapy, and surgery (mastectomy and lumpectomy) are now used to cure breast cancer. The sixth the leading cause of death from malignancy is breast cancer. While lung cancer remains the most frequent reason of cancer mortality in more industrialised areas, it is becoming the second most prevalent cause of cancer death in females in less industrialized areas [(5)].

TYPES OF BREAST CANCER

The majority of breast malignancies are carcinomas. Adenocarcinomas, which include invasive carcinoma and ductal carcinoma in situ (DCIS), are the most prevalent types of breast cancer [(6)].

Non-invasive breast cancer cells are those that remain in the ducts and do not spread to the breast's connective and fatty tissues. The majority (90%) of non-invasive breast cancer cases are caused by ductal carcinoma in situ (DCIS). LCIS, a less frequent condition that is thought to increase the chance of developing breast cancer. Breast cancer cells invade the adjacent fatty and fibrous tissue of the breast after piercing the tube and lobular wall.. Without metastatic (spreading) to the lymph nodes or other organs, oancer can be invasive [7].
Breast cancer comes in a wide range of forms, including invasive and non-invasive malignancies. Ductal carcinoma in situ and lobular carcinoma in situ are examples of non-invasive breast cancer, while invasive breast cancer includes Inflammatory breast cancer, Phyllodes tumours of the breast, invasive ductal carcinoma, invasive lobular carcinoma, Paget's disease of the nipple, locally progressed breast cancer, metastatic breast cancer, and Phyllodes tumours of the breast [8].

Etiology of Breast Cancer

It's crucial for women to undergo general health screenings to identify risk factors linked to an elevated the occurrence of breast cancer development [9]. Seven major categories may be used to classify breast cancer risk factors:

1. Age: With the growing older of the female population, the age-adjusted frequency of breast cancer is rising.

2. Gender: Women account for the majority of breast cancer cases..

3. Personal history of breast cancer: A prior primary breast cancer raises the risk of a subsequent primary cancer in the opposite breast.

4. Histologic risk factors: Breast biopsy histologic abnormalities are a significant group of breast cancer risk factors. These abnormalities include proliferative alterations with atypia and lobular carcinoma in situ (LCIS).

5. Exogenous hormone use: The two most frequent uses of therapeutic or supplementary oestrogen and progesterone are contraception in premenopausal women and hormone replacement treatment in postmenopausal women [10,11,12].

Epidemiology of Breast Cancer

The second-leading cause of cancer-related deaths among women globally is breast cancer, which affects women more frequently than any other type of cancer. Breast cancer was found in around 2.3 million females in 2020, and 685 000 people died as a consequence of the condition. It is crucial that various populations place a high focus on preventative and control measures for breast cancer. Also crucial is raising knowledge of risk factors and early identification in poorer nations [13,14]. The American Cancer Society (ACS) reports that women from different racial and ethnic groups have the following breast cancer rates:
White non-Hispanic: 128.1 per 100,000
African Americans: 124.3 per 100,000
Latino/Hispanic: 91.0 out of 100,000
Native Alaskan/American Indian: 91.9 out of 100,000
Asian Americans or Pacific Islanders: 88.3 out of 100,000 [24,25].

Symptoms of Breast cancer

Breast cancer symptoms and signs might include:
1. A breast growth or lump that feels different from the tissue around it.
2. A breast's size, shape, or appearance changing.
3. Skin changes, such as dimpling, on the breast area.
4. A nipple that was just inverted.
5. The pigment tissue around the nipple (areola) or breast skin exfoliates, scales, crusts, or flakes.
6. The skin above your breasts is red or pitted, like orange skin.

Diagnosing breast cancer

The following tests and techniques are used to identify breast cancer:

1. Breast exam: Your doctor will feel for lumps or other abnormalities in your lymph vessels in the armpit as well as both of your breasts.

2. Mammogram: Mammograms are frequently used as a breast cancer screening tool. Your doctor could advise a diagnostic mammography if an abnormality is found on a screening mammogram in order to further assess that anomaly.

3. Breast ultrasound: Ultrasound employs sound waves to generate images of inside organs at great depths. If a new breast lump is found to be a solid mass or a cyst filled with fluid, ultrasound may be performed to identify it.

4. Breast magnetic resonance imaging (MRI): A magnet and radio signals are used by an MRI machine to produce images of your breast's inside. You get a dye injection before to a breast MRI. An MRI doesn't employ radiation to produce the pictures, in contrast to other kinds of imaging procedures.

DIFFERENT APPROACHES OF NANOPARTICLES IN BREAST CANCER

Targeting Nanoparticles for Breast Cancer

Chemotherapeutic drugs are widely utilized in the treatment of breast cancer. However, the majority of anticancer medications are unable to differentiate among cancer and healthy cells, which might have harmful side effects. Additionally, medication resistance developed during chemotherapy lessens the effectiveness of the therapy. Targeted drug delivery has a lot of potential for treating breast cancer, both in terms of clinical applications and pharmacological research. An efficient therapeutic approach for treating malignant disorders is the conjugation of nanocarriers with targeted ligands. We concentrate on chemical ligands such as immunoglobulin, peptides, aptamers, nutrients, hormones, and polysaccharides that can actively target breast cancer cells [(16)].

Curcumin-loaded magnetic nanoparticles for breast cancer

Natural diphenol curcumin (CUR), which is obtained from the powdered rhizomes of Curcuma longa, has a number of biological qualities that might be advantageous, including anticancer and chemoprevention abilities. CUR may efficiently upregulate p53, p21, and p27 and downregulate cyclin E; hence, cell cycle arrest occurs in the G1 phase in these cancer cells. Additionally, CUR induces apoptosis in MDA-MB-231 cancer cells, which reduces their viability and dependence on their anchorage, and suppresses constitutive STAT3 signaling. In triple-negative breast cancer cells, CUR promotes DNA damage, improves cellular localization and phosphorylation, and modifies BRCA1. Additionally, when combined with radiation or chemotherapy medicines, CUR showed synergistic antiproliferation effects. Normal human tissues do not exhibit any discernible toxicity when exposed to CUR. However, problems with its solubility, degradation in physiological media, and fast metabolism must be resolved before CUR may be successfully introduced into the therapeutic setting. Conjugate, emulsion, lipid, polymer, and gel nanoparticle-based CUR nanoformulations (nanomedicine of CUR) have been proposed for enhancing therapeutic benefits and sensitization for chemotherapy and radiation [(17)].

Iron oxide nanoparticles

Because of its cheap rate, super paramagnetic nature, biocompatibility, and biodegradability, IONPs distinguish themselves from other NPs**.** Due to their superparamagnetic feature, which allows them to heat up when subjected to an outside magnetic field or simply be directed to a specific spot using an external magnet, they have become extremely important in the field of cancer therapy. Additionally, the only metal oxide NPs authorized for use in MRI are IONPs. Magnetite (Fe3O4) with maghemite (Fe2O3) are two magnetic phases of superparamagnetic iron oxide nanoparticles (SPIONPs) that are very promising for use in biomedicine. With the use of an external magnetic field, SPIONPs are also readily able to target tumour tissues. Other biological uses for SPIONPs include tissue-specific release of therapeutic drugs, improved MRI imaging and detection, radio sensitization, magnetic field-assisted radionuclide treatment, and in vitro diagnostics as magnetic sensing probes.

Targeted camptothecin delivery via silicon nanoparticles reduces breast cancer metastasis

High cytotoxicity and non-specificity combine to make camptothecin (CPT) a poor water-soluble chemotherapeutic agent. The epidermal growth factor receptor (EGFR)-targeting antibody (Ab) cetuximab was embedded into porous silicon nanoparticles (pSiNP) in this study to provide a soluble and precise nanoscale delivery vehicle for the management of cancer. Fabrication and characterization of targeted and non-targeted CPT-loaded pSiNP importantly, our method's surface functionalization enables directed antibody attachment via its fragment crystallizable (Fc) region, allowing the engagement of their active site with the relevant cell-surface receptor. pSiNP measured using transmission electron microscopy (TEM) has a diameter of 165 15 nm [(18)].

CONCLUSION

Human breast cancer continues to be a very hazardous and complicated condition with several unanswered concerns. Nanotechnology is a rapidly developing scientific field that has the potential to be used for imaging, monitoring, diagnosing, and delivering drugs to certain targeted tumour cells. Several approaches like Targeting Nanoparticles, Curcumin-loaded magnetic nanoparticles, Iron oxide nanoparticles etc. have been developed over the years. The new platform for nanoparticles will continually be created by ongoing efforts by scientists, researchers, and other medical professionals working in the field of nanotechnology. Nanotechnology will benefit the field of medicine in the near future, in addition to cancer, where it will likely be used more frequently.

REFERENCE:

1. Tagde P, Najda A, Nagpal K, Kulkarni GT, Shah M, Ullah O, Balant S, Rahman MH. Nanomedicine-Based Delivery Strategies for Breast Cancer Treatment and Management. International Journal of Molecular Sciences. 2022 Mar 5;23(5):2856.
2. Momenimovahed Z, Salehiniya H. Epidemiological characteristics of and risk factors for breast cancer in the world. Breast Cancer: Targets and Therapy. 2019;11:151.

3. Nikdouz A, Namarvari N, Shayan RG, Hosseini A. Comprehensive comparison of theranostic nanoparticles in breast cancer. American Journal of Clinical and Experimental Immunology. 2022;11(1):1.
4. Berríos-Torres SI, Umscheid CA, Bratzler DW, Leas B, Stone EC, Kelz RR, Reinke CE, Morgan S, Solomkin JS, Mazuski JE, Dellinger EP. Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. JAMA surgery. 2017 Aug 1;152(8):784-91.
5. Ghoncheh M, Mahdavifar N, Darvishi E, Salehiniya H. Epidemiology, incidence and mortality of breast cancer in Asia. Asian Pacific journal of cancer prevention. 2016;17(sup3):47-52.
6. Henry NL, Shah PD, Haider I, Freer PE, Jagsi R, Sabel MS. Chapter 88: Cancer of the Breast. In: Niederhuber JE, Armitage JO, Doroshow JH, Kastan MB, Tepper JE, eds. Abeloff's Clinical Oncology. 6th ed. Philadelphia, Pa: Elsevier; 2020.
7. Sharma GN, Dave R, Sanadya J, Sharma P, Sharma K. Various types and management of breast cancer: an overview. Journal of advanced pharmaceutical technology & research. 2010 Apr 1;1(2):109.
8. Arjaans M, Schröder CP, Oosting SF, Dafni U, Kleibeuker JE, de Vries EG. VEGF pathway targeting agents, vessel normalization and tumor drug uptake: from bench to bedside. Oncotarget. 2016 Apr 4;7(16):21247.
9. Chun MC. Breast Cancer: Symptoms. Risk Factors, and Treat-ment, Medical News Today Available from: https://www. medicalnewstoday. com/articles/37136. php.
10. White AJ, Bradshaw PT, Hamra GB. Air pollution and breast cancer: a review. Current epidemiology reports. 2018 Jun;5(2):92-100.
11. Gucalp A, Traina TA, Eisner JR, Parker JS, Selitsky SR, Park BH, Elias AD, Baskin-Bey ES, Cardoso F. Male breast cancer: a disease distinct from female breast cancer. Breast cancer research and treatment. 2019 Jan;173(1):37-48.
12. Sharma GN, Dave R, Sanadya J, Sharma P, Sharma K. Various types and management of breast cancer: an overview. Journal of advanced pharmaceutical technology & research. 2010 Apr 1;1(2):109.
13. Wang T, Cao C, Gavahi M, Sadri M, Rong X. Using Nanotechnology for Diagnosis and Treatment of Breast Cancer: A Review. Indian Journal of Pharmaceutical Sciences. 2022 Apr 20:237-45.
14. Clark BZ, Onisko A, Assylbekova B, Li X, Bhargava R, Dabbs DJ. Breast cancer global tumor biomarkers: a quality assurance study of intratumoral heterogeneity. Modern Pathology. 2019 Mar;32(3):354-66.
15. Kitamura M, Nakayama T, Mukaisho KI, Mori T, Umeda T, Moritani S, Kushima R, Tani M, Sugihara H. Progression potential of ductal carcinoma in situ assessed by genomic copy number profiling. Pathobiology. 2019;86(2-3):92-101.
16. Alqaraghuli HG, Kashanian S, Rafipour R. A review on targeting nanoparticles for breast cancer. Current pharmaceutical biotechnology. 2019 Nov 1;20(13):1087-107.
17. Yallapu MM, Othman SF, Curtis ET, Bauer NA, Chauhan N, Kumar D, Jaggi M, Chauhan SC. Curcumin-loaded magnetic nanoparticles for breast cancer therapeutics and imaging applications. International journal of nanomedicine. 2012;7:1761.
18. Thoidingjam S, Tiku AB. New developments in breast cancer therapy: role of iron oxide nanoparticles. Advances in Natural Sciences: Nanoscience and Nanotechnology. 2017 Jun 2;8(2):023002.