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A STUDY OF RISK FACTORS AND PREVENTIONS OF BREAST CANCER INITIATION AND PROGRESSION

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ABSTRACT
The evaluation of saponin-rich fractions for anticancer activity can lead to the discovery of new chemical entities or derivatives with improved efficacy and reduced side effects. Nature often presents a diverse range of structurally distinct compounds, and saponins are no exception. By analyzing different plant sources, it becomes possible to identify novel saponins or modify existing ones to enhance their anticancer potential. This can contribute to the development of safer and more effective treatments for cancer patients. The evaluation of saponin-rich fractions can also provide valuable insights into the underlying mechanisms of action. Understanding how these compounds interact with cancer cells and the molecular pathways they modulate can uncover new targets for drug development. This knowledge can help in the design of more specific and selective therapies, minimizing off-target effects and improving overall treatment outcomes. The evaluation of saponin-rich fractions from selected plants contributes to the conservation and sustainable use of plant resources. By identifying specific plants that contain valuable anticancer compounds, efforts can be made to cultivate and harvest them responsibly. This approach ensures the long-term availability of these plant sources for therapeutic purposes while minimizing the impact on the environment.

KEYWORDS: Risk Factors, Breast Cancer, Initiation and Progression

INTRODUCTION

Disease and mortality are increasingly being caused by non-communicable conditions including cancer and cardiovascular disease as a result of an aging global population coupled with unhealthy lifestyles and more medical intervention. Cancer is the leading cause of death in the world, and throughout the 20th and into the 21st century, it has been a disease that is poorly understood, feared, and ultimately lethal. By the year 2030, it is expected that there would be around 21.4 million new cases of cancer and 11.2 million new deaths from cancer per year. This condition, which is really a collection of more than a hundred different diseases, is characterized by the uncontrollable multiplication of abnormal cells inside the body, which leads to tissue invasion, metastatic progression, and, finally, death. Cancer is characterized by a number of molecular and genetic alterations, including aberration, inadequate programmed cell death, excessive proliferation, attack angiogenesis, and metastasis. Depending on the primary cell type(s) that are damaged, over a hundred distinct types of cancer have been identified so far. These include: skin cancer, cervical cancer, lung cancer, leukemia, breast cancer, prostate cancer, etc. Cancer is third among leading causes of mortality in developing nations, behind

cardiovascular disease and infectious illnesses. As a result, it is a serious challenge for healthcare systems, and both the management and treatment of these conditions are labor-intensive.[1]

Early identification by mammographic screening and tumor-specific systemic treatments such surgery, chemotherapy, radiation therapy, monoclonal antibody, hormone therapy, and immunotherapy have allowed for the successful management of BC and other cancer-related disorders. Despite these therapeutic possibilities, cancer survivors are at an increased risk of dying because of cancer-related complications, difficulties in early identification, and the high expense of therapy. In light of these restrictions, more effective and less risky therapeutic strategies are required to increase the likelihood of survival from BC with little or no therapy-related side effects and at a reduced financial outlay.[3]

Preventative measures that use pharmaceutical and other novel approaches to morbidity reduction deserve praise. We urgently need a method that can eradicate BC with sufficient efficacy and decreased toxicity at least in high-risk populations. Plants have been revered as a primary resource for the treatment of diseases from prehistoric times, but no one knows for sure when or when this practice first began; ancient stories, however, provide a possible clue that it may have originated in the Stone Age.There is evidence to suggest that various plant components were widely employed by the indigenous and pastoral cultures of ancient Egypt, India, China, Greece, and Rome to treat illness and restore vitality. WHO estimates that between 75 and 90 percent of the world's population relies on traditional medicine, most often plant medications, to meet their primary health care needs. Traditional medicines, which include many of the pharmaceuticals on this list, are often derived from plants.

BREST CANCER (BC)

Despite major advancements in research, BC remains a major health linked problem and calls for increased biological explorations. In both the developed and the developing nations, it is one of the most commonly diagnosed forms of cancer in women, and it is the second greatest cause of cancer-related death among women. Approximately 50-75% of breast cancers originate in milk ducts, with the remaining 10-15% developing in lobules and a negligible percentage in other breast tissues.

Metastatic cancers like BC spread to unrelated sites such as the liver, bone, brain, and lungs and are largely incurable. The incidence of breast cancer in India continues to rise. It is estimated that there would be roughly 2,00,000 additional cases by the end of the year 2030. The current rate of BC in the United States is one in eight women, but experts predict that by 2024, this might rise to one in seven. One out of every 28 Indian women will develop breast cancer sometime in their lives. This rate is significantly greater in poorer countries, where it is estimated to be between 55 and 58 percent. [13]

Recent upsurge in cases of BC in young women have piqued the interest of scientists looking into the phenomenon. There is strong evidence to suggest that BC is a leading cause of cancer-related mortality among women under the age of 45. More cases were reported in high-

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income countries, while more deaths occurred in low- and middle-income countries (LMICs). The gap between new cases and fatalities is expanding, suggesting that screening is essential and that this cancer is often diagnosed too late to save lives.Therefore, according to WHO, the foundation for controlling BC remains superior BC results and resilience in the face of premature discovery.

Due to early detection by mammographic screening and the use of systemic adjuvant treatment, the incidence of metastases and fatalities of BC patients have decreased in recent years.

Treatment with chemotherapy increased 15-year survival rates by 10% in women under the age of 50 and by 3% in women over the age of 50. However, even after 20 years after initial diagnosis, survivors have a greater chance of reappearance; they also exhibit an increased risk of weight gain and other co-morbidities, such as cardiovascular diseases or metabolic disorders. [14]

Pathogenesis of breast cancer

Breast tumors develop from duct cells that divide uncontrollably; these tumors can be either benign or metastatic carcinomas. Unwanted ductal proliferation, a necessary step in tumor development, is stimulated by a wide variety of carcinogens. Macrophages and the subsequent formation of stromal cells both play critical roles in the onset and development of breast cancer. Macrophage-produced inflammation in DNA aids angiogenesis and immune evasion by cancer cells in breast cancer. DNA methylation patterns differ between healthy and tumor-related microenvironments, suggesting that factors other than mutations may contribute to carcinogenesis. Tumor researchers are currently analyzing cancer stem cells (CSCs), a newly discovered type of dangerous cell. These CSCs are linked to the onset, progression, and recurrence of cancer. Unlike most other cancers, breast cancer stem cells (BCSCs) do not often emerge from the basal stem cell compartment. More research is needed to learn more about BCSCs and find better ways to get rid of them.[15]

There are primarily two theoretical assumptions for the onset and development of BC: the CSCs theory and the stochastic theory. The cancer stem cell hypothesis postulates that all tumor types arise from the same pool of underlying cancerous cells. Rearrangement of genetic information and altered expression of several gene products are found in stem cells due to both genetic and non-genetic alterations (Figure 1.A). All tumor types, according to the stochastic hypothesis, originate from a single cell type, such as a stem cell, progenitor cell, or differentiated cell (Figure 1. B).

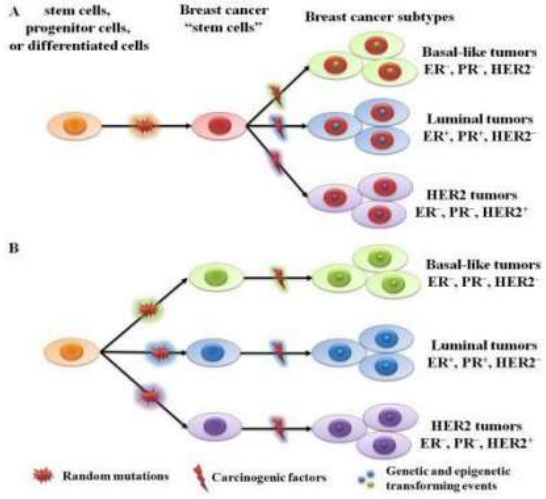

Figure 1. Two hypothetical theories of breast cancer initiation and progression

(A) All subtypes of tumor are derived from the same stem cells or progenitor cells.

(B) Each tumor subtype is initiated from a single cell type (stem cell, progenitor cell, or differentiated cell).

Risk factors for breast cancer

Risk factors are characteristics that are associated with an increased probability of developing a disease such as cancer. Up to this point, many risk factors that have a role in the development of BC have been identified. The following are some of the causes of BC:[16]

1. Age

There is a strong correlation between age and the prevalence of BC; as one gets older, their likelihood of developing the disease also rises.

According to SEER data, the lifetime risk of developing BC in American women is 1 in 8, 1 in 202 from birth to age 39, 1 in 26 from age 40 to 59, and 1 in 28 from age 60 to 69.[17]

2. Family history

The majority of breast cancer cases have a familial component. There is an increased risk of breast cancer in women who have a family history of the disease. If a woman's mother or sister has breast cancer, she is more likely to have the disease herself. A woman's risk ratio for developing breast cancer is 1.80 for one affected first-degree relative, 2.93 for two, and 1.90 for three or more.

2.1. Genetic causes

The BRCA1 and BRCA2 breast cancer genes are rare and are associated with a lifetime risk of between 40 to 85% of developing BC. There is an increased risk of breast and ovarian cancer in younger women who carry the BRCA1 gene. The lifetime risk of developing BC for people who carry the BRCA1 or BRCA2 alterations is from 65% to 81% and 45% to 85%, respectively. BC susceptibility is also associated with mutations in the genes encoding EC adherin (CDH-1) and p53 (a tumor suppressor). The tumor suppressor gene CHEK2 and the homozygous form of ATM both pose a low risk. These moderate genes account for a 20% to 40% lifetime risk of developing BC. Further research is needed despite the fact that numerous low-threat general genes have been identified, primarily by genome-wide related exams.

Endogenous hormone exposure and Reproductive factors

The risk of developing breast cancer and how long a woman can expect to live are both influenced by the natural rhythm of a woman's endogenous estrogen production.

1. Early menarche Menarche

BC can develop in women before and after menopause, and early onset is a risk factor for both. those whose menstrual periods began before the age of 13 were at around twice the risk for developing hormone-related malignancies compared to those whose menstrual periods began after the age of 27.

2. Parity and age at first full term pregnancy

Nulliparous women, in contrast to parous women, face a greater risk of developing BC. When comparing primiparous women to nulliparous women, a younger first delivery age has a protective effect, while a higher first delivery age confirms a large threat of BC.[19]

Breast feeding

The evidence suggests that breastfeeding can act as a barrier to the onset of BC.

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Breastfeeding has been shown to lessen the risk of disease by 4.3% annually.

Testosterone

Higher levels of circulating testosterone in postmenopausal women are associated with an increased risk of cancer.

Age at menopause

The risk of developing breast cancer increases by 3% for every year that menopause is delayed, and by 17% for every 5 years that it is delayed. [20]

Exogenous hormone exposure

Hormone-receptor positive breast cancer (BC) is quite common among those who take hormone replacement treatment (HRT). When comparing HRT users to non-users in terms of BC growth, users face a much greater risk. Using just estrogen after menopause in women without a uterus can greatly lower the incidence of breast cancer and does not interfere with breast cancer detection. HRT's duration and timing are also crucial factors in BC risk. The closer a woman is to menopause when she starts HRT, the higher the risk. Maximum risk is associated with long-term (> 5 years) use of HRT, but short-term use of progestin-estrogen therapy does not appear to significantly improve risk. [21]

Life style and dietary cause

High dietary fat and excess weight are risk factors for breast cancer in sedentary postmenopausal women. Similarly, drinking alcohol can lead to breast cancer. Risk factors for breast cancer include having a first child after the age of 30, having a pregnancy terminated early, using oral contraceptives, taking hormone replacement medication after menopause, and not getting enough exercise. Smoking was found to be a more significant risk factor in the development of BC.

Radiation

The risk of developing BC is greatly increased by exposure to radiation, which can come from a variety of sources, including medical therapy and nuclear explosions. Radiation therapy for chest wall cancer in children increases the risk of BC. Surviving patients of childhood cancer who underwent radiation therapy are at increased risk of developing BC later in life.

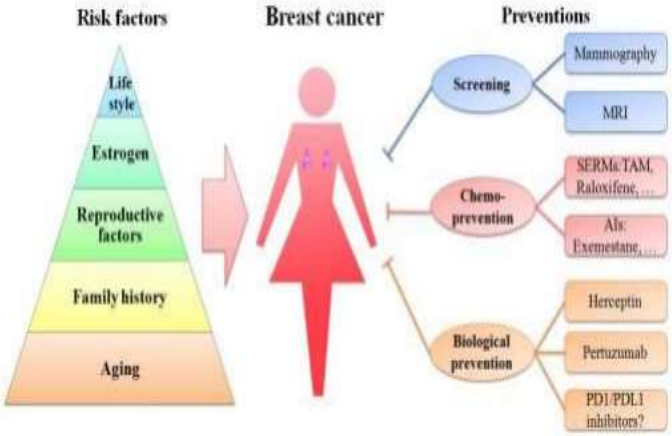

Figure 2 Schematic diagram of risk factors and preventions of breast cancer

Types of breast cancer

1. Based on occurrence, invasiveness and pathology

Depending on whether parts of the breast (lobules, ducts, or tissues) are damaged, many distinct types of BC can arise. BCs can be further subdivided into sarcomas and carcinomas based on the cell types that are typically involved. Cancer of the breast (BC) sarcomas are relatively rare and develop in the stromal components of the breast, which include blood vessel and myofibroblast cells. On the other hand, breast carcinomas originate in the epithelial cells that line the lobules and the terminal ducts that are responsible for milk

production. There are three basic categories of BCs based on pathological features and invasiveness: non-invasive, invasive, and metastatic.[23]

1.1. Non-invasive (or in situ) breast cancer

The term "in situ" refers to cancer that has not spread beyond the site where it first appeared. Intraductal carcinoma in situ (DCIS) is a common kind of non-invasive (90%) breast cancer. There is a greater risk of metastasis for in situ carcinomas. Increased risk of invasive breast cancer is associated with LCIS, a rare form of breast cancer that develops in the milk glands (lobules). [24]

1.2. Invasive or infiltrating breast cancer

Breast ductal carcinomas begin in cells that have broken away from their normal ducts and lobules and have invaded neighboring connective and fatty tissue to form a tumor. Invasive carcinomas, when left untreated, can metastasize to lymph nodes and other organs. Invasive BCs are further subdivided into the following categories based from the cell and tissue types they affect.

Less common types of breast cancer

1. Inflammatory breast cancers (IBC)

Only 1-5% of all BCs are this extremely aggressive kind. Symptoms of inflammatory breast cancer include breast enlargement, breast redness or purpleness, and breast skin thickening. Most cases of IBC go undetected on mammograms because no breast lumps occur. In addition, IBCs develop rapidly, are more damaging, and spread rapidly than more common types of BCs. Women who are younger and heavier are more likely to get IBC. Metastasis occurs in a high percentage of patients with IBCs, making treatment more challenging.

2. Breast cancers in men and children and adolescents

Bowel cancers (BCs) in men account for less than one percent of all cases of the disease. Most male patients with breast cancer (BC) also express IDC and ER. Lymphoma and alveolar rhabdomyosarcoma are two examples of metastatic malignancies that disproportionately affect children.

Stages of breast cancer

Stages of breast cancer are as follow:

Stage 0: cancer in situ, specifically ductal carcinoma in situ (DCIS) or lobular carcinoma in situ (LCIS).

Stage I: Breast cancer at its earliest stages, when the tumor is less than 2 centimeters in diameter and has not spread beyond the breast.

Stage II IA: Both the tumor's diameter and the number of lymph nodes it metastasized to under the arm are less than 2 centimeters. Lymph nodes in the area around the breastbone on the affected side became involved.

IIB: The tumor is 2–5 cm in diameter and has spread to between 1-3 lymph nodes in the armpit. The tumor is larger than 5 centimeters in diameter and hasn't grown outside the breast, or it has spread to lymph nodes close to the breastbone on the same side as the tumor.

Stage III IIIA: The tumor is no more than 5 centimeters in diameter, and it has spread to between 4 and 9 lymph nodes in the armpit, or it has caused inflammation in at least one lymph node close to the breastbone. The tumor is more than 5 centimeters in diameter and has

metastasized to as many as nine lymph nodes near the breast bone.

IIIB: Inflammatory breast cancer occurs when a tumor invades the breast tissue and spreads to the chest wall. It can impact more than 10 lymph nodes in the armpit or enlarge in the lymph nodes near the collar bone, but they can be any size.

CONCLUSION

The saponin rich fraction of A. calamus rootrhizome, A. lebbeck bark, C. fimbriata leaves, and H. annuus flower petals showed antiproliferative, antiangiogenic, and apoptotic effect in many in vitro investigations. Saponin rich fractions did not produce any DNA damage or toxicity in normal cells, as shown by the lack of a detectable increase in chromosomal abnormalities in normal human blood lymphocytes. Thus, modern research validates the traditional use of Acorus calamus, Albizia lebbeck, Caralluma fimbriata, and Helianthus annuus, and authenticates their potential application in cancer therapy.

REFERENCES

1. Makhoahle Paksio, Mashele Samson, "IN VITRO ANTICANCER ACTIVITY OF PAPPEA CAPENSIS MEDICINAL PLANT FROM MOKOPANE", Archives • 2021 • vol.2 • 234-241
2. Modarresi Chahardehi, A., Arsad, H., Zafirah Ismail, N., & Lim, V. (2021). Low cytotoxicity, and antiproliferative activity on cancer cells, of the plant Senna alata (Fabaceae). Revista de Biología Tropical, 69(1), 317-330. DOI 10.15517/rbt. v69i1.42144
3. Nelson, V.k., Sahoo, N.K., Sahu, M. et al. In vitro anticancer activity of Eclipta alba whole plant extract on colon cancer cell HCT-116. BMC Complement Med Ther 20, 355 (2020). https://doi.org/10.1186/s12906-020-03118-9
4. ShridharC.GhaganeSrideviI.PuranikVijayM.KumbarRajendraB.NerliSunilS.JalalpureMurigendraB.HiremathShivayogeeswarNeelagundRavindranathAladakatti, "In vitro antioxidant and anticancer activity of Leeaindica leaf extracts on human prostate cancer celllines", Integrative Medicine Research, Volume 6, Issue 1, March 2017, Pages 79-87
5. Soumya, T., Lakshmipriya, T., Klika, K.D. et al. Anticancer potential of rhizome extract and a labdane diterpenoid from Curcuma mutabilis plant endemic to Western Ghats of India. Sci Rep 11, 552 (2021). https://doi.org/10.1038/s41598-020-79414-8
6. Kauroo, S., Govinden-Soulange, J., Ranghoo-Sanmukhiya, V.M. et al. Extracts of select endemic plants from the Republic of Mauritius exhibiting anti-cancer and immunomodulatory properties. Sci Rep 11, 4272 (2021). https://doi.org/10.1038/s41598-021-83461-0
7. F. Beheshti, A. A. Shabani, M. R. Akbari Eidgahi, P. Kookhaei, M. Vazirian, M. Safavi, "Anticancer Activity of Ipomoea purpurea Leaves Extracts in Monolayer and

Three-Dimensional Cell Culture", Evidence-Based Complementary and Alternative Medicine, vol. 2021, Article ID 6666567, 14 pages, 2021. https://doi.org/10.1155/2021/6666567

8. Ly, H.T., Truong, T.M., Nguyen, T.H. et al. Phytochemical screening and anticancer activity of the aerial parts extract of Xanthium strumarium L. on HepG2 cancer cell line. Clin Phytosci 7, 14 (2021). https://doi.org/10.1186/s40816-021-00252-w
9. Purnamasari R, Winarni D, Permanasari AA, Agustina E, Hayaza S, Darmanto W. Anticancer Activity of Methanol Extract of Ficus carica Leaves and Fruits Against Proliferation, Apoptosis, and Necrosis in Huh7it Cells. Cancer Inform. 2019 Apr 19;18:1176935119842576. doi: 10.1177/1176935119842576. PMID: 31037025; PMCID: PMC6475848.
10. Muhammad Imran Qadir, Muhammad Ali and Zubair Ibrahim, "Anticancer activity of Morus nigra leaves extract", International Pharmaceutical Abstracts, Open J-gate, Science Citation Index Expanded, SCOPUS and Social Sciences Citation Index ISSN: 1991-0088; DOI: 10.3329/bjp.v9i4.19783
11. Azhagu MS. Phytochemical Analysis and Anticancer Activity of Azadirachta Indica Ethanolic Extract against A549 Human Lung Cancer Cell Line. J Biomed Res Environ Sci. 2021 Apr 16; 2(4): 280-285. doi: 10.37871/jbres1225, Article ID: JBRES1225
12. Padalia, H., Chanda, S. Antioxidant and Anticancer Activities of Gold Nanoparticles Synthesized Using Aqueous Leaf Extract of Ziziphus nummularia. BioNanoSci. 11, 281–294 (2021). https://doi.org/10.1007/s12668-021-00849-y