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Breast Cancer Treatment Relying on Herbal Bioactive Components

Dr. Keshamma E[1], Dr. Anil Kumar[2], Ritesh Jha[3], Vandana Sonaji Amle[4], Gitanjali Sambhajirao Dudhate[5], Dr. Divyakant Patel[6], Purabi Saha[3] and Roshan Kumar[7]

[1]Associate Professor, Department of Biochemistry, Maharani Cluster University Palace Road, Bangalore – 560001, INDIA.

[2]Ex. Research Scholar, Department of Botany, DDU Gorakhpur University Gorakhpur-273009, INDIA.

[3]Department of Pharmacy, Uttaranchal Institute of Pharmaceutical Sciences, Uttaranchal University, Dehradun-248007, Uttarakhand, INDIA.

[4]Master of Pharmacy, School of Pharmacy, S.R.T.M.U. Nanded, INDIA.

[5]Department of Pharmaceutics, Indira college of Pharmacy Vishnupuri Nanded-431605, INDIA.

[6]Professor, Sharda School of Pharmacy, Pethapur, Gandhinagar, Gujarat, INDIA.

[7]Assistant Professor, Guru Nanak College of Pharmaceutical Sciences, Dehradun, Uttarakhand, INDIA.

[7]Correspondence Author: rjroshan244@gmail.com

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ABSTRACT

Use of herbs and plants in cooking and medicinal dates back thousands of years. In this overview, we look at the many plant species that still have immune-boosting and cancer-fighting properties. Carotenoids, flavonoids, ligands, polyphenolics, terpenoids, sulphides, lignans, and plant sterols are only some of the many active phytochemicals found in different types of herbs. There are a number of mechanisms through which these phytochemicals exert their effects. They either prevent cell division or stimulate the synthesis of a protective enzyme such as glutathione transferase. The cancer-fighting and cholesterol-lowering effects of mevalonate are counteracted by the volatile oils and plant extracts from various herbs and plants.

Keywords- Breast cancer, Herbs, Bioactive, Medicinal plants.

I. INTRODUCTION

Humans have been exploring different plant species for thousands of years in an effort to treat illness and improve overall health. Therefore, they have found many bioactive compounds in plants that have great medicinal promise. Flavonoids, carotenes, alkaloids, and phenolics are four of the most studied plant chemicals having medicinal effects, including anticancer potential[1]. Cancer is a genetic disease caused by the uncontrolled proliferation of abnormal cells within the body and their spread to other parts of the body; breast cancer is one of the most common varieties[2-5]. Breast cancer exemplifies the wide range of female-specific diseases. When it comes to cancer diagnoses, breast cancer is second only to skin cancer[6-9]. Luminal A, luminal B, basal-like (which is similar to TNBC) and human epidermal growth factor receptor 2 breast cancers are the four main subtypes (HER2). Receptors for the female hormones oestrogen (ER), progesterone (PR), and human epidermal growth factor 2 (HER2) are frequently associated to many different types of cancer. Immunohistochemistry (IHC) of certain receptor expressions, such as ER/PR positivity or negativity and HER2 positivity or negativity, allows for the classification of breast cancer into distinct subtypes[10-14]. TNBC accounts for 15–25% of all breast cancer cases and is the most aggressive kind. TNBC is difficult to treat because it lacks ER, PR, and HER2 receptor expression, making it resistant to hormone and HER2-therapies. Metastatic breast cancer can spread to other parts of the body. As a result of metastasis, breast cancer has a very high mortality rate[15-18].

By 2021, the WHO estimates that there would have been 685,000 deaths and 2 million new cases of

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breast cancer over the world. Breast cancer risk factors include age, having a family history of the disease, being overweight, being exposed to radiation, having a faulty BRCA1 or BRCA2 gene, not having a family history of the disease, having a normal or low-risk PTEN, ATM, TP53, CHEK2, STK11, or PALB2 gene, and having a faulty CHEK2 or PALB2 gene[7]. Risk factors include having no children, having only one child, not breastfeeding, using postmenopausal hormone therapy or oral contraceptives, eating a diet rich in saturated fat and low in fibre, drinking excessively, and smoking. A case study done in Mexico City found that obese or overweight breastfeeding mothers are at an increased risk for getting breast cancer[19-23].

There is a lot of work being done all around the world to find ways to both prevent and treat breast cancer. Technology advancements led to the manufacture of synthetic medicines, while the traditional use of medicinal plants gradually faded into obscurity. However, in recent decades, as people have become aware of the severe side effects these synthetic pharmaceuticals cause, interest in the possibilities of phytomedicine has increased. Plant extracts are preferred over chemotherapy drugs due to the lower risk of side effects associated with natural remedies[24-26].

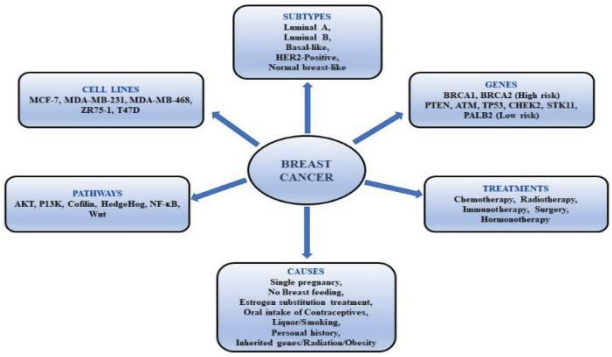

Fig: 1 Finding the genes, processes, and environmental factors that put people at risk for developing breast cancer.

The many breast tumours, their etiologies, their related genes, and the cell lines in which they grow are all described in Figure 1. Breast cancer cannot be cured with natural remedies, but a nutritious diet, regular exercise, and enough sleep can help[27-29]. The flavonoid quercetin has been demonstrated to reduce the incidence of breast cancer, and it can be found in abundance in onions, eggplant, garlic, potatoes, tomatoes, lettuce, peppers, apple, oranges, and fragrant herbs. Plants are now recognised as a safe and reliable source of compounds that can inhibit cancer's growth. The evidence that plant extracts can induce apoptosis (programmed cell death) in cancer cells continues to rise. Toxic compounds found in plants range in number. Many plants contain toxic compounds like ricin, which can be used as a poison. This necessitates giving adequate time and effort to the mining of the possible chemicals[30-34].

A recent study found that inactivity was a factor in about 9 percent of breast cancer cases, supporting findings from the European Code Against Cancer. People who exercised for roughly three hours each week had a reduced risk of acquiring breast cancer, according research published in the European Journal of Oncology Nursing. Therefore, exercise can help reduce the risk of breast cancer[35]. Less fat on the body is associated with a reduced risk, especially in postmenopausal women. Surgery, inpatient care, radiation therapy, chemotherapy, and hormone therapy are all viable alternatives for treating breast cancer. Conversely, the side effects of chemotherapeutic drugs can be reduced by using them in conjunction with bioactive compounds found in plants[36-39].

II. MATERIAL & METHODS

We use Pubmed, Publon, Scopus, and User Generated Content in our search (UGC). For instance, breast cancer describes the unchecked growth and proliferation of cells that initially manifest in the breast tissue. Cancers are typically referred to by the organ or tissue from whence they first appeared. The breast is composed of two primary types of tissue: glandular tissues and stromal (supporting) tissues. Glandular tissues contain the milk-producing lobules and ducts, while stromal tissues are made up of the breast's fatty and fibrous connective tissues. Breasts include lymphatic tissue, which helps the immune system rid the body of waste and excess fluids. Many different forms of tumours can develop in various parts of the breast. Breast tumours are typically generated by benign (not malignant) mutations. For instance, fibrocystic change is a benign illness that causes breast lumps, thickening, discomfort, pain, cysts (accumulated packets of fluid), fibrosis (the growth of scar-like connective tissue), and fibrosis in women. Cancers of the breast typically begin in the lining of the ducts (ductal cancers). Some cancers (lobular cancers) begin in the cells that line the lobules, whereas others (skin cancers) originate in other organs.

Types of Breast Cancer

Ductal Carcinoma In-situ: Ductal carcinoma in situ (DCIS), sometimes called intraductal carcinoma, is a kind of breast cancer in which abnormal epithelial cells proliferate within a duct's basement membrane but do not invade the surrounding tissue. If the basement membrane layer was broken, DCIS would develop into invasive breast cancer. DCIS is considered a precursor to invasive breast cancer. A neoplastic growth of epithelial cells restricted to the mammary ductal-lobular system, DCIS is "characterised by modest to marked cytologic atypia and an inherent but not necessarily obligate tendency to progression to invasive breast cancer," according to the World Health Organization[40-42].

DCIS is a heterogeneous group of lesions that vary in their clinical presentation, genetics, biomarkers, morphologic characteristics, and clinical propensity to

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progress to invasive breast cancer, while being categorised. Screening mammography has been shown to increase the rate at which microcalcifications, found before the disease becomes clinically apparent, are diagnosed. In order to confirm a DCIS diagnosis, however, a tissue sample is required[43-47]. Radiation therapy, hormone therapy, and surgery are all potential components of a comprehensive treatment plan for DCIS.

Invasive breast Cancer: Invasive breast cancer encompasses a wide spectrum of cancer types. The many histological types each have their own unique characteristics in terms of clinical manifestation, imaging findings, histopathology, biomarkers, and prognosis and prediction. Presently, histopathological features are the primary criterion for classifying invasive breast cancer[48-50]. A variety of rare entities have been documented, however the most majority are aggressive carcinomas that lack differentiation. Novel genetic insights into invasive breast cancer and the function of the stromal milieu are only two examples of the new ideas that have emerged as a result of recent research and technological breakthroughs[17]. The most recent classification of breast tumours by the World Health Organization has been updated based on the correlation of histology and genetic data, which reflects our improved understanding of the pathophysiology of invasive breast cancer[51-53]. Cancers that originate in the medullary ducts of the breast are referred to as medullary carcinomas, and they are part of the larger category of tumor-infiltrating lymphocyte-rich breast malignancies. Reversed polarity in tall cell carcinoma is recognised as a different entity due to the presence of unique IDH2 mutations. Some genetic information concerning breast cancer and the function of lymphocytes that infiltrate tumours are discussed in this article, in addition to a review of classic prognostic variables, new histological entities, and categorization modifications[54-57].

Triple-negative breast cancer: There are six distinct subtypes of the diverse cancer known as TNBC. Immunomodulatory (IM), basal-like 1 (BL-1), basal-like 2 (BL-2), and mesenchymal (M) are the subtypes (MSL). Gene expression profiles are used to classify these groups. Among these shared features between BL-1 and BL-2 is the considerable gene expression that occurs during cell division and the advancement of the cell cycle[58]. Nonetheless, BL-1 shows significant gene expression in the growth factor signalling pathway, while BL-2 shows high gene expression in the DNA response pathway, which includes DNA replication and repair activity. In contrast, genes involved in immune cell functions such as the natural killer cell pathway, the TH1/TH2 pathway, cytokine signalling, the B cell receptor (BCR), and antigen processing are highly expressed in immunomodulatory (IM). In addition, it is well-established that mesenchymal stem-like and mesenchymal subtypes exhibit a higher level of gene expression in the pathways of extracellular receptor contact, cell motility, and cell differentiation. Nonetheless, MSL is distinct from other mesenchymal subtypes in that its claudins (3, 4, and 7) gene expression is low[22]. Malignancies of the MSL subtype, discovered by Herschkowitz et al., are thus categorised as claudin-low tumours. Finally, the LAR subtype shows high expression of androgen receptor-related genes, including co-activators and hormone-regulated pathways. However, TNBC molecular subtypes were reclassified into four tumor-specific subtypes including BL1, BL2, M, and LAR after Lehmann et al. found that IM paired with MSL TNBC subtypes were presented by infiltrating lymphocytes and tumor-associated mesenchymal cells[59-62].

Inflammatory breast cancer: Isolated breast cancer is a rare kind of invasive breast cancer that has spread locally according to the TNM staging criteria. It is estimated that between 2% and 4% of breast cancer cases in the United States can be attributed to this factor. Inflammatory breast cancer (IBC) is uncommon but contributes to 7 percent of all breast cancer deaths. Clinically, this condition is differentiated by the presence of diffuse induration of the skin that has an erysipeloid appearance; nevertheless, no underlying tumour is seen in most cases[63-66]. The most up-to-date guidelines from the American Joint Committee on Cancer (AJCC) define IBC as a separate clinicopathologic entity when erythema and edoema involve at least one-third of the breast and can extend to the other breast, the mediastinum, the upper extremities, and the neck.

Primary IBC is characterised by a high degree of angiogenic invasion. Normal experimental studies have looked at the impact of the p53 tumour suppressor gene, cytokines, and other genetic variables on hormone receptor status and genetic alterations. Proteins that act as receptors for hormones and other indications of cancer The vast majority of IBCs lack hormone receptors. Negative oestrogen receptor (ER) and progesterone receptor (PGR) in breast cancer is associated with a worse chance of survival and a shorter disease-free period. Human epidermal growth factor receptor 2 is also overexpressed by IBCs, and their proliferation rates are rather high (HER 2). Potentially, these molecular markers could be used to single out patients who have a worse prognosis[67-70].

Genetic alterations: Half or more of IBCs have lost heterozygosity. Frequent deletions include those on chromosomes 17q, 13q, 11, 8P, 6P, and 3P.

P53 tumor suppressor gene (TSG): p53 protein accumulation or p53 TSG mutations have been found in 20-50% of malignant breast tumours. Hereditary breast cancer syndromes such as familial breast and ovarian cancer typically involve these atypicalities (e.g., Li-Fraumeni syndrome). According to the results of multiple observational studies, individuals with nuclear overexpression and the P53 gene mutation had an 8.6-fold higher risk of death than patients without both mutations, as well as larger tumours and more extensive sickness at the time of diagnosis. The simultaneous and strong interaction between ER expression and prognostic

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variables is also demonstrated. Patients who demonstrated both ER negative and p53 nuclear overexpression had an 18-fold greater risk of dying compared to women who only displayed p53 nuclear overexpression[71-73].

New gene mutations: Overexpression of the RhoC GTPase oncogene was more common in IBCs (90 vs. 38%), as was deletion of WISP3 (WNT1-inducible-signaling pathway protein 3). (80 versus 21 percent).

Cytokines: Most inflammatory cytokines, including interleukin-12, interleukin-1, and interferon-gamma, are produced, but only at low levels, making the term "IBC" deceptive. Inflammatory breast cancer is more likely to have extensive blood vessels because it is angiogenic and angioinvasive. There is an increase in the production of VEGF, IL-6, and IL-8 from these cells. Transfected human mammary epithelial cells release more of these cytokines when the RhoC GTPase gene is overexpressed. RhoC GTPase is uniquely associated with invasive breast cancer[74-76]. Activation of vascular endothelial growth factor-3, in particular by VEGF-D in IBC, is involved in the lymphotactic process by contributing to the development of new lymphatic arteries in close proximity to the tumour.

Paget's Disease: Paget's disease of the breast is an unusual manifestation of breast cancer in postmenopausal women. Although invasive cancer might develop, ductal carcinoma in situ is usually the underlying breast disease (DCIS). As the symptoms are similar to those of other skin rashes a woman could experience, it is easy to overlook or misdiagnose[77-80]. This case study exemplifies the importance of an interdisciplinary team in the detection and management of breast Paget disease. Paget's disease of the breast can be categorised in the same way as other breast cancers using the TNM classification and staging method. As a result, having Paget disease of the breast has little bearing on the development of the underlying breast cancer. If invasive breast cancer or DCIS is absent at the same time as Paget disease, the condition is classified as Tis (Paget disease). Breast cancer's underlying cause is a major factor in determining the best course of treatment. Historically, a simple mastectomy has been the gold standard for treating PDB, whether or without an underlying tumour. Recently, conservative therapy for the breast has become the gold standard for treating DCIS (BCT). The treatment of invasive breast cancer lacks standardisation. The presence of PDB in addition to a palpable tumour or certain mammographic abnormalities is often indicative of an advanced stage of breast cancer. Positive axillary lymph nodes and/or the presence of a secondary tumour are more likely than they would be in the absence of a first tumour[81]. The underlying lesion needs to be excised by a nipple-areolar complex. If a substantial local excision can be performed with negative margins and excellent cosmetic results, then BCT is the preferred treatment, followed by whole breast radiation therapy (RT).

Some Common herbs that are used for the treatment of breast Cancer

Echinacea:

It is the Asteraceae family that includes the popular flowering plant echinacea. It's a wild aromatic plant that's cultivated in the Great Plains and the East Coast of North America and also manufactured in Europe. When it comes to herbal remedies, the three most common types of Echinacea are Echinacea purpurea, Echinacea angustifolia, and Echinacea pallid. However, E. purpurea is widely used in scientific study and clinical practise. Echinacea is commonly referred to by a variety of common names, including purple coneflower, Kansas snakeroot, and black Sampson. It has been discovered that E. purpurea raises the number of natural killer cells in the mice used in the studies[82]. As time goes on, E. purpurea may prove to be an effective cancer treatment. Echinacea's presence of flavonoids has been shown to boost the immune system. This is supported by the findings of Winston et al., and flavonoids stimulate lymphocyte activity, which in turn enhances macrophage phagocytosis, natural killer cell activity, and the induction of interferon assembly. They lessen the risk of radiation and chemical side effects. And it even extends the lives of those who have already reached a terminal stage of cancer. The cytokine production of macrophages can be stimulated by consuming commercially available Eechinacea juice. Less clear effects are seen on the 7 activation and proliferation of T-cells and B-cells. Several of the plant's constituents are responsible for Echinacea's specialised effects on the immune system[83].

Garlic:

Among the most important European studies, researchers found that eating onions and garlic was associated with a lower chance of developing breast cancer. One further large Italian population study confirmed that eating more allium vegetables rich in flavones and flavonols was associated with a reduced risk of breast cancer. Korean researchers have found that reducing their intake of onions and garlic results in fewer instances of breast cancer[84]. Allium species, such as garlic, have anti-carcinogenic qualities due in part to the presence of organosulfur compounds (ajoene, diallyl sulfide, diallyl disulfide, diallyl trisulfide, diallyltetrasulfide, dipropyltetrasulfide, among others). Ajoene has been found to kill triple-negative (ER-/PR-/HER2-) breast cancer cells by preventing them from folding proteins correctly. Animal studies have shown that diallyl disulfide is effective at reducing carcinogen-induced tumours. Also, diallyl disulfide has been demonstrated to induce apoptosis (programmed cell death) in both ER+/PR+ and triple negative breast cancer cells[85]. It has been discovered that ductal carcinoma in situ (DCIS) with micro-invasion sites is sensitive to diallyl trisulfide, which triggers the cells in those places to die. In addition to slowing the progression of breast cancer, diallyl trisulfide has been shown to prevent the invasion and dissemination of cancerous breast cells. Specific

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growth and metastasis inhibition of triple-negative breast cancer cells by diallyl trisulfide has been reported[86].

Curcumin:

Chemicals originating from plants are widely employed in oncology due to their vast therapeutic properties and minimal toxicity. Various biological and molecular characteristics of cancer cells are the focus of natural substances. Studies have shown that curcumin affects signalling pathways in cancer cells, reduces the creation of proteins linked to treatment resistance, and boosts the efficacy of anti-tumor drug[87]. Curcumin's capacity to reverse drug resistance pathways makes chemotherapy-resistant cells more vulnerable to treatment. Keyvani-Ghamsari et al. shown the efficacy of curcumin in treating cancer.

Experiments in the lab on different colorectal cancer cell types have shown that curcumin inhibits cell growth and promotes death by interacting with multiple molecular targets. Curcumin has also been used in dietary formulations intended to ward off colon cancer. Both in vitro and in vivo studies have shown that these compounds have anti-cancer properties against colon cancer and the inflammation it causes[88]. This study provides promising evidence that curcumin may effectively protect mice from developing colorectal cancer. Positivistic hope is provided to people by this quality. Unfortunately, there hasn't been a lot of clinical trials involving humans, so the outcomes are all over the place. Future trials with large enough samples sizes are needed to investigate several open questions, such as the optimal dosage, bioavailability, optimum indicators, and potential toxicity[89]. Curcumin has been shown to inhibit lung cancer cell growth and survival by inducing apoptosis, autophagy, and cell cycle arrest. By targeting multiple signalling pathways, including NF-B and the epidermal growth factor receptor, curcumin may enhance radiation therapy's effectiveness in the treatment of lung cancer. Nanocarriers loaded with curcumin improve the compound's bioavailability, cellular uptake, and anticancer activity. Patients with adenomatous polyposis were given oral curcumin in a study by Cruz-Correa et al. Curcumin's safety and effectiveness in treating patients with adenomatous polyposis were examined in this study. In this study, 44 individuals with adenomatous polyposis received 1500 mg of oral curcumin twice day for a period of 12 months. The findings demonstrated that there was no discernible difference between those receiving oral curcumin and placebo[38]. Using a histological diagnosis, Howells et al. investigated 24 patients with metastatic colorectal cancer who were older than 18 in 2019. Questionnaires were used to evaluate these patients' quality of life and neurotoxicity. According to the findings, curcumin is a safe and well-tolerated addition to FOLFOX chemotherapy for people with metastatic colorectal cancer. Overall, the findings imply that curcumin can be used in combination with other drugs to suppress and control malignancies, ameliorate clinical symptoms, and stop tumour growth and metastasis. Vasodilation, cell proliferation, and metastasis are all inhibited by this substance, which also affects other molecular pathways[90].

Green Tea:

However, when conducting a meta-analysis of observational research, confounding became a significant concern, especially when sample sizes were small. For this reason, we performed a subgroup analysis based on location, case group origin, severity of NOS, and case count to evaluate the impact of these and other potential confounders on our findings. The way a study is set up can also have an impact on how the association between GT use and breast cancer risk plays out[93]. With their ability to properly establish the connection between factors and disease, cohort studies also have additional benefits from an epidemiological and etiological perspective. Since breast cancer was a chronic disease, it was difficult to do a thorough long-term follow-up of the study's participants in a cohort study. Loss to follow-up was also inevitable, which meant that withdraw bias would emerge. There may be time and cost savings as well as reduced bias in case-control studies as compared to other research designs. There is a rundown of these regulations. To begin, there is considerable variation in the study's overall estimate, which must be taken into account. There is a wide range of variation in factors such as case count >500, NOS grade 6, hospital-based controls, and region[91]. The use of random-effect models in this meta-analysis does not make it any easier to explain these differences. Second, we need to be cognizant of publication bias; researchers hiding the results of tiny studies with unfavourable results should be. Publication bias may have inflated the reported link between GT intake and breast cancer risk. Thirdly, potential biases such as information bias or misclassification bias could not be entirely removed in this study because our conclusions are dependent on the outcomes of case-control studies. Finally, the majority of the studies included in this meta-analysis did not specify when the development of breast cancer occurred, making it difficult to tell if GT was eaten by patients before or after the disease developed[94].

Cymbopogon Citratus:

Interfering with the cell cycle is a proven method for combating cancer because it has a broad range of effects, including on cell growth, differentiation, and death. Progression through the cell cycle requires precise and stringent regulation by a number of cellular regulatory components, including cyclin-dependent kinases (CDKs) and cyclins[95]. Cell cycle arrest can be induced by a large number of medications by affecting regulators at discrete checkpoints in the cell cycle. Important regulators of G1 cell cycle progression, CDK4/6 and CDK2, were linked to cyclins D1/D3 and E. The heptamethine cyanine dye (IR-783) caused a G0/G1 arrest in breast cancer cells, as reported by downregulation of cyclin D1, cyclin E, and cyclin-dependent kinase 2 (CDK2). Similarly, Gao et al. found

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that -Cryptoxanthin induced a G0/G1 arrest in SGC-7901 cells and AGS cells via the downregulation of cyclin E, cyclin D1, and CDK4, CDK6. In this study, a significant G0/G1 cell cycle arrest was detected by flow cytometry. Cyclin D1 and cyclin dependent kinase 4 levels were dramatically decreased in CCP-treated MDA-MB-231 cells. These results showed that the cell cycle of MDA-MB-231 cells was arrested at the G0/G1 phase when CCP was present[96].

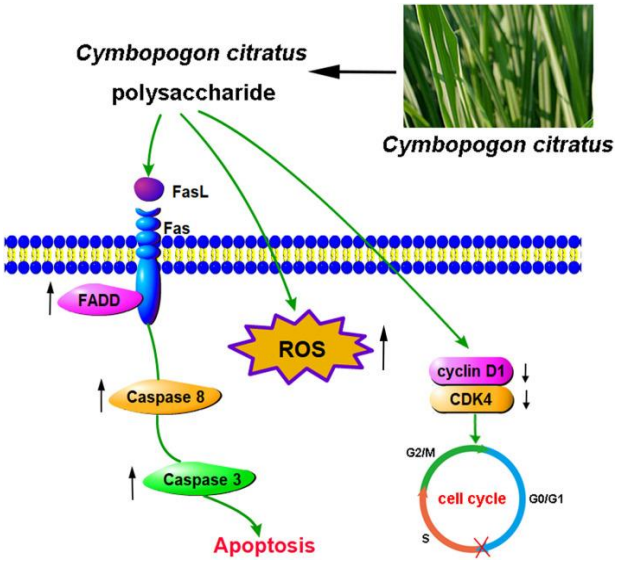

Fig. 2: Potential molecular pathways involved in cell cycle arrest and apoptosis in MDA-MB-231 cells are mediated by CCP.

Eclipta alba:

Eclipta alba is a well-known plant with significant ethnomedical usage in the Indian subcontinent. The Indian Ayurvedic pharmacopoeia includes the herb on its list of recommended remedies because of its hepatoprotective properties. In the present work, nonmetastatic human MCF 7, metastatic human MDA-MB-231, and metastatic mouse 4T 1 cell lines were used to investigate the anti-breast cancer effect of AEEA. Each cell line's proliferation was shown to be inhibited by AEEA in a concentration-dependent fashion[97].

Apoptosis, also known as genetically regulated programmed cell death, occurs throughout embryonic development, normal ageing, and pathological settings including preserving tissue homeostasis. Apoptosis is characterised by distinct morphological changes, such as the breakdown of plasma membrane asymmetry and attachment, plasma membrane blebbing, cytoplasmic and nuclear condensation, and internucleosomal DNA cleavage[98].

Morphological study of breast cancer cells was performed to ascertain whether the cytotoxic effect was linked to apoptosis. The results demonstrated that the hallmarks of apoptosis, including cell shrinkage, membrane ruffling, and blebbing, are induced by AEEA administration. Fluorescent microscopic examination of AEEA-treated breast cancer cells revealed phosphatidylserine externalisation, an essential feature of early apoptosis, by the interaction of Annexin V FITC, which interacts with phosphatidylserine and produces green fluorescence[53]. Here we see that apoptosis was more prevalent in treated cells compared to controls. Examining cells under a fluorescence microscope stained with propidium iodide reveals that AEEA administration causes cell death by apoptosis, membrane blebbing, and chromatin condensation. Treatment with AEEA causes karyopyknosis and chromatin condensation in the nucleus, both of which lead to programmed cell death, as shown in further studies utilising breast cancer cells stained with Hoechst 33342. In conclusion, microscopy results showed that AEEA induces apoptosis-mediated cell death in breast cancer cells that have been treated[99].

The mitochondria in your cells are responsible for producing the energy that keeps your body going in an aerobic environment, but they can also be a source of apoptotic cell signals. Several mitochondrial proteins are directly involved in this signalling process. As the mitochondrial membrane potential decreases, signals are released that initiate the programmed cell death process known as apoptosis[100]. Loss of mitochondrial membrane potential was quantified using the positively charged fluorescent dye rhodamine 123. The current study demonstrated that a dose-dependent decrease in mitochondrial membrane potential triggered a cascade of events leading to death in cells treated with AEEA through the loss of fluorescence induced by the externalisation of Rhodamine 123 from the mitochondrial matrix.

III. CONCLUSION

This review elaborated on the nine herbs' chemopreventive and chemotherapeutic effects on breast cancer. These herbs were found to have anti-cancer effects in both in vitro and in vivo studies, with results showing that they inhibited tumour growth, spread, angiogenesis, angiogenesis, apoptosis, and cell survival pathways. The herbs' active ingredients have a variety of molecular effects, including on nuclear factor-B, vascular endothelial growth factor, and Bcl-2, all of which play important roles in the development of breast cancer. Despite their biological activity, herbs like turmeric and thyme include compounds with poor absorption and pharmacokinetic characteristics, such as curcumin and thymoquinone. On the other hand, echinacea's medical efficacy is diminished by the fact that it inhibits cytochrome P450 enzymes in both vitro and in people. Fortunately, these limitations can be overcome with the help of nanotechnology-based liposome carriers and formulations.

It has been found that the anti-cancer effects of certain herbs can be multiplied when combined with those of standard chemotherapy drugs including tamoxifen, doxorubicin, 5-fluorouracil, and paclitaxel. There was a

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parallel improvement in the efficacy of chemotherapy drugs and a reduction in their hazardous side effects. It would be interesting to see if the chemo-preventive and chemotherapeutic effects of curcumin nano-formulation may be amplified by co-delivering chemotherapeutic medications. More study involving large-scale clinical studies is needed to determine the safety of combining the nanoformulation of the active chemical with standard chemotherapy treatments.

Most of the chemopreventive activities of these herbs have been studied in a variety of human cancer cell lines and, to a lesser extent, animal tumour models. Care should be used in interpreting the findings until it can be validated by data from clinical studies, although it does appear that these herbs have broad anti-cancer properties as medicines. Thoughts in Concluding Additional research into the known and undiscovered biologically active components of these plants should take quality control, toxicity and safety profiles, and the assessment of their pharmacodynamics and pharmacokinetics into account. More clinical research including trials and cohort human studies is needed to provide substantial proof of the medicinal benefits of these herbs.

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