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Research Article

Natural Products Use For The Management Of Breast Cancer: A Review

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ABSTRACT

Breast cancer is highly prevalent among women worldwide. Preventing breast cancer is more advantageous than treating it. The treatment of breast cancer using chemotherapy and/or radiation therapy is highly challenging and often leads to adverse side effects due to the intricate and diverse molecular Factors that influence the onset of the illness. Throughout the ages, individuals have employed botanical extracts to address many ailments, including breast cancer. Due to their low toxicity, herbal drugs are a dependable choice for cancer treatment. Moreover, due to their easy accessibility and affordable cost, a significant proportion Women who have been diagnosed with breast cancer readily adopt herbal remedies. Over the past decade, numerous plants and their components have demonstrated significant potential in inhibiting the growth of breast cancer cells, as observed in both laboratory and animal studies. Yet, the lack of randomized clinical trials raises uncertainty regarding the positive effects of these treatments on breast cancer. Aims to present findings on the potential utilization of specific herbal products for the treatment or prevention of breast cancer. Furthermore, it provided information on the potential chemotherapeutic function of these phytocompounds, specifically highlighting their anticarcinogenic mechanism.

Key terms: Breast cancer, phytochemicals, phytoestrogens, and herbal remedies

1.INTRODUCTION

According to WHO, Cancer is an escalating worldwide health concern and ranks as the second most common cause of death globally, after cardiovascular diseases. About 25% of all cancer cases affecting females globally are identified as breast cancer, making it The most common type of cancer in women. Currently, there are commendable research endeavors aimed at identifying the precise molecular process underlying the progression of breast cancer, identifying new therapeutic targets that have lower toxicity, and uncovering the etiology of the illness.[1,2] Undoubtedly, these attempts are optimistic considering the huge rise in overall survival for various forms of breast cancer in the last ten years. The significant advancements treating breast cancer have resulted in a remarkable 25% decrease in death rates associated with the condition since 1990. Chemotherapy is the predominant technique of cancer treatment, utilizing cytotoxic chemicals to eradicate cancer cells. However, these compounds exert an influence on both malignant and non-malignant cells, resulting in a range of undesirable consequences during or after treatment.[3,4] Currently, research is mostly focused on discovering herbal medications that precisely target cancer cells in order to address these concerns. Furthermore, breast cancer distinguishes itself from other types of cancer by encompassing a multitude of genetic disorders that impact many pathways. Medicinal plants are utilized for the purpose of preventing and treating diseases. These complexities contribute to the development of various diseases with different clinical outcomes. Consequently, the response of a patient to a specific chemotherapy prescription can differ, and an

insufficient treatment approach can exacerbate the toxicity.[5,6] Multiple recent studies have demonstrated that various herbal compounds possess distinct cytotoxic properties, which makes them potentially effective in chemotherapy. Meanwhile, numerous herbal products have demonstrated the ability to improve quality of life, reduce stress, and prevent or alleviate the negative effects of treatment.[7,8]

Breast cancer and its potential effects

Worldwide, breast cancer is the leading cause of cancer-related fatalities in women. By 2040, 3.05 million cases and 6.99 million fatalities are predicted based on the current trajectory. Breast cancer will affect 10% of women. Epidemiological data show that both industrialized and developing nations are seeing an increase in breast cancer cases. Environmental and lifestyle factors are the primary causes of breast cancer, accounting for just 10-15% of instances that are inherited. Main risk factors for breast cancer are being over 50, having a family history of the disease, and certain characteristics of a woman's reproductive history, such as early menstruation, never having given birth, conception later in life, and menopause later in life.[9,10]

The development, course, and management of breast cancer are influenced by its molecular characteristics

Cancer arises from a sequence of molecular events. Cancer could therefore result from aberrant cell division and proliferation caused by DNA or protein damage involved in the cell cycle. Molecular changes leading to overgrowth of cells result in abnormal cell death, division, blood vessel formation, and spread of cancer.[11,12]
Metastases, invasive carcinoma, and DCIS develop as a result of excessive duct growth. Based on molecular pathways, two categories of breast cancer can be distinguished: HER2 amplification (ErbB2) and ERα and PR expression. The genes, which encode the proteins BRCA-1 and BRCA-2, are essential for both genomic stability and DNA repair. Breast cancer risk is elevated by 15–20 times by mutations in these genes. The p53 protein, which regulates the cell cycle and starts apoptosis, is encoded by the tumor suppressor TP53.[13,14] Breast cancer frequently modifies signaling pathways like NF-κβ and the JAK/STAT system. Treatment decisions are aided by the breast cancer molecular expression classification. Which patients receive hormone therapy or chemotherapy/targeted medications is determined by the aforementioned indicators. Effective cancer treatments involve signaling system alteration and intervention in the modulation stages of carcinogenesis, which include initiation, promotion, and progression.
Medication for breast cancer slows the cell cycle by changing cell shape or inducing programmed cell death, prevents DNA damage to genetic material, and blocks aberrant cell development pathways.[15,16] The estrogen hormone receptor, which stimulates cancer cell proliferation with circulating estrogens, is implicated in the majority of breast cancer cases. Current therapies aim to eliminate estrogen from breast tumors that are ER-positive. Tamoxifen is an effective selective estrogen receptor modulator (SERM). Tamoxifen inhibits the expression of estrogen via altering the structure of the estrogen receptor (ER). However, because of its estrogenic effects on tissues and organs, tamoxifen, like selective estrogen receptor modulators (SERMs), can also lead to secondary cancer and cardiovascular disease.[17,18] Letrozole and anastrozozole compete with aromatase to lower the production of estrogen. It is unknown how these therapies may affect your health in the long run.[19,20]
The HER2 gene is overexpressed in about 20% of women with breast cancer, which increases the disease's aggressiveness and lowers survival. Trastuzumab and lapatinib are the only medications that block the signals associated with HER2 development and proliferation. Enzyme-mediated DNA damage is also a useful cancer treatment strategy. The anthracycline medication doxorubicin increases DNA-topoisomerase II covalent complexes by forming intercalation bonds with DNA base pairs. Topoisomerase II is blocked by this. Additional anti-cancer medications harm microtubules, impeding the metaphase-to-anaphase transition. Next, the cell experiences either apoptosis or mitotic arrest.[21,22] By attaching to the vinca or taxoid-binding domains and severing the link between the tubulin β- and α-subunits, vincristine and vinorelbine prevent the production of microtubules. In mitosis, the cell is stopped. These therapies have increased survival and decreased the death rate from breast cancer. However, adverse effects might vary from mild and transient to serious and fatal.[23,24]

Adverse effects of chemotherapy in breast cancer

The efficacy of chemotherapy in curing cancer remains uncertain. In instances of metastatic breast cancer, it additionally reduces the likelihood of recurrence and extends the patient's lifespan while improving their overall quality of life. Nevertheless, the utilization of it is associated with various risk factors or detrimental consequences; certain of which are small and temporary, while others have the potential to progress into life-threatening ailments. A common side effect of chemotherapy drugs is their indiscriminate toxicity, resulting in the destruction of both cancer cells and healthy cells in the bone marrow, hair follicles, and other essential organs.[25,26] Moreover, chemotherapy drugs possess the capacity to inflict significant damage on both brain and immune system cells, so rendering the patient more vulnerable to infections and cognitive deterioration. These adverse effects may be temporary, resolving within a few months following the completion of the treatment. Chemotherapeutic medicines can cause infertility, which is a significant and long-lasting side effect. Chemotherapeutic drugs that induce ovarian damage might result in menopausal symptoms, including irregular menstrual cycles and vaginal dryness, which can render pregnancy unattainable. Additionally, the

utilization of aromatase inhibitor medications as supplementary treatment triggers premature menopause in women who have not yet reached menopause, causing a state of reduced estrogen levels that decreases bone density and contributes to the development of osteopenia or osteoporosis.[27,28] Furthermore, cardiac abnormalities might arise as a result of long-term damage induced by chemotherapy, which can also increase the risk of developing secondary cancers such as leukemia or marrow neoplasms. Chemotherapy-induced cardiotoxicity is a prominent side effect of cancer treatment that contributes to the increased mortality rate in cancer patients, given the high prevalence of cardiovascular problems in this population. Congestive heart failure (CHF), a condition that occurs more frequently in both young and old adults, is mostly caused by cardiotoxicity. Reports indicate that breast cancer patients aged 65 to 70 who received adjuvant anthracycline treatment had a significantly higher occurrence of congestive heart failure (CHF). In a separate study, it was shown that Doxorubicin, a frequently prescribed chemotherapy drug, was responsible for congestive heart failure (CHF) in a significant 26% of breast cancer patients. During the early stages after chemotherapy, there is a heightened susceptibility to developing MN.[29,30] Moreover, under certain conditions, chemotherapy medicines might potentially disrupt a patient's typical psychological condition. The main reason for the occurrence of side effects related to conventional chemotherapy is the drugs' lack of ability to selectively target cancer cells. Most frequently employed chemotherapy drugs have detrimental effects on vital organs and healthy cells, hence limiting the dosage that can be administered. This elucidates the low therapeutic index of cancer medications. Various strategies are being employed to enhance the effectiveness of anticancer drugs in tackling this issue.[31,32]

Utilization of herbal remedies and ethnomedicine for the treatment of cancer

Throughout the entirety of human existence, plants have provided fundamental necessities such as sustenance, attire, housing, and remedies, all of which have played a crucial role in the survival and advancement of the human species. These are ancient medical systems that originated from plants and have been employed by individuals to address various health conditions.[33,34] Traditional herbal medicines have become popular because they are inexpensive, readily available, and have few or no negative side effects. In recent years, there has been an increasing focus on performing plant research globally with the aim of identifying pharmaceuticals or drug-like chemicals from historically used medicinal plants. In addition, certain naturally derived plant compounds, such as quercetin, resveratrol, curcumin, and others, have shown promising anti-cancer effects and are increasingly being used as adjuncts to chemotherapy. In addition, naturally occurring chemicals have a tendency to be more harmful to abnormal or diseased cells while being less poisonous to healthy cells. This may be attributed to the abundance of medications available in the current market, which possess structural resemblances to naturally existing compounds.[35,36]

Herbal compounds possess many anticancer effects, such as antioxidant, anti-inflammatory, antimutagenic, and apoptosis-inducing capabilities, which can contribute to the early detection and prevention of cancer. Out of the 136 anticancer drugs licensed for global usage from 1981 to 2014, almost 83% were either herbal compounds or derived from them. Several antineoplastic drugs are currently employed for the treatment of breast cancer. Despite the efficacy of herbal remedies in treating breast cancer and its associated consequences, there is a lack of progress in moving them through preclinical and clinical stages.[37,38]

Herbal treatments for the prevention of breast cancer

Breast cancer can be prevented. Both healthy breast cells and cancerous breast epithelium grow and multiply mostly because of the presence of estrogens. Estrogen receptor-positive breast cancers comprise approximately 40-70% of all cases. Phytoestrogens, which are plant-derived compounds that resemble estrogen, were initially proposed as a means of preventing cancer. Phytoestrogens exhibit a lower affinity for the hormone receptor due to their structural similarities with the mammalian hormone estrogen. Plant estrogens are categorized based on their chemical structure.[39,40] Soy and soy products are rich in isoflavones. In Asian cultures, the consumption of dietary isoflavones can reach levels as high as 20-80 mg per day. Additionally, epidemiological research revealed a modest 30% reduction in the likelihood of developing breast cancer among women who had a greater proportion of lignan in their diet.[41,42] Consequently, physical activity holds significant importance in the prevention of breast cancer. Phytoestrogens not only inhibit estrogenic activity, but they also activate GPR30, also known as GPER-1. GPR30 is a G-protein coupled receptor that is considered a new estrogen receptor and is involved in various estrogen-dependent diseases, such as breast cancer. Nevertheless, the specific mechanism of action of phytoestrogens remains uncertain and relies on various factors, such as their molecular structure, metabolism, and relative abundance compared to naturally occurring estrogen.[43,44]

These phenolic compounds are present in numerous plants that have nutritional and medicinal properties. Several phenolic compounds have a wide array of biological effects, making them effective in preventing the development of cancer and inhibiting the process of carcinogenesis.[45,46]

Ginseng

Ginseng is a type of perennial herb that falls under the Panax genus and Araliaceae family. Ginseng is made up of different botanical species. Panax japonicus and Panax ginseng. Panax ginseng, also referred to as Korean or Asian ginseng, is extensively grown in China and Korea. On the other hand, Panax quinquefolius, originally cultivated in the United States and Canada, is not as commonly utilized.[47,48]

Ginseng is classified according to its processing method and boasts a pleasant taste. Ginseng Radix Rubra is a type of ginseng that has been steamed once during processing. After undergoing nine rounds of steaming, it is commonly known as Black ginseng. Ginseng Radix Alba is the term used to describe dried ginseng. Ginseng plants contain the main active ingredient, Panax ginseng Meyer, in their thin roots, which are rich in ginsenosides. Ginsenosides are triterpene steroidal saponins that can have various sugar moieties, including xylose, glucose, rhamnose, or arabinose, depending on their type, number, and location. The molecular makeup of the aglycones distinguishes the three primary categories of ginsenosides found in ginseng. Let's start with the protopanaxadiol group. This group is also known as diols. The second category includes the triols, specifically the protopanaxatriol group. The oleanane group, primarily composed of Ro, is the third type.[49,50]

The varying concentrations of ginsenosides present in the Panax species enable the distinction between different species. There are several key ginsenosides found in Panax ginseng root. These ginsenosides make up over 90% of the overall composition of the root. In comparison to American ginseng, Panax ginseng contains higher levels of Rg1 compared to Rb1, leading to an increased Rg1/Rb1 ratio. The American ginseng root is primarily composed of its main constituents, which make up over 70% of its makeup. Given the diverse chemical structures of ginsenosides, they exhibit varying pharmacological effects and mechanisms of action. These ginsenosides, have caught the attention of researchers due to their potential in cancer treatment. The composition of ginseng root includes a significant amount of water-soluble polysaccharides, which are both neutral and acidic, in addition to ginsenosides.[51,52]

Ginsenoside Red ginseng contains a crucial bioactive component known as Rh2, which is the primary active saponin responsible for the plant's anti-cancer properties. For the purpose of examining the inhibitory effect of Rh2 on the growth of breast cancer cells in a laboratory setting. Their study uncovered that Rh2's impact on the proliferation of the MCF-7 human breast cancer cell line is influenced by the dosage. This was achieved by modifying genes that are essential for the growth of malignancies and do not possess methyl groups. Through the utilization of promoter methylation, Rh2 effectively reduces the levels of C3orf67-AS1, a noncoding RNA that has been recently discovered, thereby exerting its potent anti-cancer properties.[53,54]

Through its ability to induce cell cycle arrest in the G(0)/G(1) phase, Rh2 demonstrates a strong inhibitory impact on the growth, which varies depending on the concentration. Through the inhibition of Rh2 effectively suppresses both cell lines. The complexes are regulated by p27(Kip1) and p15(Ink4B), which play a role in inhibiting the associated kinases. Consequently, there was a decrease in pRb phosphorylation and cyclin/Cdk complex kinase activity.[55,56]

The ginseng compound A main active ingredient in heat-processed ginseng is Rg3. It is necessary to stop cancer cell proliferation. In lab studies, 20(S)-Rg3 influences MDA-MB-231 and MCF-7 breast cancer cell proliferation. This drug lowers cyclin D1 and cyclin A and pauses G-1 cells. Two recent studies showed Rg3 suppresses breast cancer cell growth. It alters tumor-associated genes. Research shows that Rg3 impacts biological processes.[57,58]

Numerous studies have examined Rg3's anti-cancer apoptotic effect. RG3 generated reactive oxygen species to activate caspase-3 and destroy poly (ADP-ribose) polymerase in breast cancer cells. Rg3 upregulates Bax and downregulates Bcl-2. In another study, Rg3 suppresses NF-κB signaling and deactivates Akt and ERK kinases, leading to breast cancer cell death. Cell growth and cycle progression decrease. The apoptotic properties of Rg3 impact the stability of p53, leading to increased NF-κB activation.[59,60]

Breast cancer development depends on IGFs, especially IGF-1. In an animal model, Rg3 decreases IGF-1 to inhibit tumor growth and angiogenesis. Chen et al. found that 20(S)-Rg3 dramatically decreased breast cancer cell CXCR4 expression. The CXCR4 receptor and its ligand CXCL12 in metastasis must be studied to study breast cancer cells. Rg3 reduces CXCR4 expression to inhibit bone, lung, and lymph node metastasis.[61,62]

Figure 1. Ginseng

Ginseng Interaction with Anti-Cancer Drugs

In breast cancer models, few research has studied the effects of Rg3 and chemotherapy. In nude mice with MCF-7 xenograft, oral 20(s)-ginsenoside Rg3 enhanced paclitaxel bioavailability and inhibited breast tumor growth. A separate trial gave mice capecitabine, a new drug, fluorouracil (5-FU), and Rg3. Capecitabine toxicity was reduced, medication resistance was lowered, and breast cancer survival rates improved in mice. In mice, Rg3 reduced microvasculature density and VEGF expression to enhance capecitabine's antiangiogenic effects.[63,64]

Garlic

Garlic, scientifically known as Allium sativum, is a perennial plant with a bulbous structure. Grown in mild climates, this plant is highly valued for its intense flavor and captivating aroma. This enhances the flavor quite nicely. Garlic is classified into two main subspecies. One is soft-necked garlic, which encompasses varieties. Garlic contains a variety of sulfur-containing compounds. Just as a microbiologist would observe, the enzyme alliinase is responsible for converting alliin, the primary bioactive compound, into allicin, the pungent odor that characterizes garlic. Garlic is packed with a variety of beneficial compounds, such as steroidal and phenolic chemicals, carbohydrates, fiber, proteins, and trace minerals like selenium. Garlic contains lipid-soluble allyl sulfur compounds like S-allylmercaptocysteine, diallyl trisulfide, and diallyl disulfide, which have various biological effects.[65,66]

In 1990, the US Cancer Institute initiated the Designer Food Program. brought attention to the cancer-fighting properties of garlic. Numerous preclinical research has shown the potential of garlic and its organosulfur components in inhibiting the formation of organ tumors induced by carcinogens. Garlic's allylsulfide compounds have shown potential in inhibiting tumor growth in both laboratory and living organism studies. These compounds have the ability to impact molecular pathways associated with cancer. These methods involve scavenging free radicals, slowing down angiogenesis, preventing DNA adducts, and controlling cell proliferation.[67,68]

These effects encompass programmed cell death, slowing down of cell division, and activation of cancer-neutralizing enzymes. Research has shown that diallyl disulfide has a positive impact on eicosapentaenoic acid, a substance that has been found to suppress breast cancer. Additionally, it has been found to counteract the effects of linoleic acid, a substance that promotes the growth of breast cancer cells. The effectiveness of this inhibition relies on the quantity of garlic extract used and the duration of exposure. This suppression triggers programmed cell death and halts the cellular division process.[69,70]

Figure 2. Garlic

Garlic Interaction with Anti-Cancer Drugs

Dialyl disulfide has been demonstrated in recent animal research to inhibit the proliferation of breast cancer cells. This compound triggers programmed cell death, increases the production of protective enzymes and inhibits the oxidation of p53. In laboratory experiments, garlic with elevated selenium levels demonstrated superior inhibition of breast cancer cell growth compared to substances containing sulfur.[71,72]

Black Cohosh

Presenting the alluring Black Cohosh, an exquisite blossom belonging to the famous Ranunculaceae botanical family. Prepare to be captivated by its exquisite aesthetics and magnetic allure. Discover the extraordinary capacity of the root, containing a unique blend of triterpene glycosides, phenolic acids, alkaloids, and tannins. Utilize the potential of nature's most exquisite components. Discover the diverse array of vital secondary chemicals and physiologically active components found in this context. Uncover the remarkable capabilities of triterpene glycosides.[73,74] It is important not to ignore the notable phenylpropanoids, particularly isoferulic acid which is of great significance. These examples provide only a small preview of the wonders that nature possesses! Discover the remarkable effectiveness of phytoconstituent found in the rhizome, as they demonstrate their exceptional biological capacities. Discover the intriguing world of polyphenolic compounds! Explore the intriguing realm of Fukiic acid, piscidic acid, and caffeic acid derivatives. Fifteen remarkable

substances have been identified following meticulous chemical investigation. Prepare yourself to be astounded! Discover the remarkable capabilities of Black Cohosh, a captivating botanical wonder containing the exceptional chemical compound formononetin. Introducing Remifemin, a high-quality extract derived from rhizomes that is gaining significant attention in the United States. Explore the inherent effectiveness of Remifemin, now available without standardization. Do not miss out on this incredible opportunity to enhance your entire well-being.[75,76]

Uncover the remarkable capabilities of black cohosh! This remarkable herb has long been extensively utilized to treat dysmenorrhea, hot flashes, and pre-menopausal pain. Indulge in the calming advantages of black cohosh and alleviate any discomfort you may be experiencing. Explore the definitive remedy tailored just for ladies undergoing perimenopause and enjoy the respite you rightfully deserve. Say goodbye to those bothersome hot flashes and embrace a life of comfort and tranquility. Discover the unique qualities immediately. Acquire knowledge regarding the typical symptoms encountered by individuals during menopause and those diagnosed with breast cancer. Discover the remarkable benefits of black cohosh extracts! Alleviate hot flashes, anxiety, sleeplessness, and other symptoms associated with peri-menopause using this natural remedy. Black cohosh provides solace and assistance to individuals diagnosed with primary breast cancer. Bid farewell to any discomfort and embrace a substantial enhancement in your quality of life.[77,78]

Discover the remarkable capabilities of isoflavones and polyphenols found in black cohosh, as they unleash their exceptional biological effects. Explore the intriguing impact of black cohosh phytoestrogens on the hypothalamus GnRH pulse generator estrogen receptors, resulting in a balanced and synchronized array of estrogenic actions. Uncover the potency of organic components in revitalizing equilibrium inside your physique and encounter the splendor of equilibrium. Explore the significant influence of Black Cohosh as it delicately interrupts and molds the serotonergic processes controlled by selective serotonin reuptake inhibitors. Explore the remarkable advantages of this exceptional plant at this now! Explore the extraordinary capacity of the body's innate defense mechanisms to suppress cell growth and enhance general health.[79,80]

Discover the intriguing findings of many clinical research that have investigated the remarkable potential of black cohosh. Explore the notable advantages of this botanical in alleviating hot flashes for ladies who have received breast cancer therapy. Explore the thrilling benefits that await you. Discover the fascinating domain of black cohosh and its remarkable capacity to reduce hot flashes. Various research has yielded varying results, offering valuable information regarding the effectiveness of this exceptional natural medicine. Examine the fascinating outcomes of various research, with some demonstrating substantial reductions and others revealing no noteworthy alterations in comparison to a placebo. Discover the remarkable benefits of black cohosh! While scientific research on its cancer-fighting properties is limited, this herb has shown efficacy in alleviating hot flashes, anxiety, and other symptoms typically associated with breast cancer. Explore the calming advantages of black cohosh for organic alleviation. Maximize the therapeutic efficacy of the treatment by conducting meticulously designed clinical trials, with a specific emphasis on breast cancer.[81,82]

Figure 3. Black Cohosh

Curcuma longa

Curcuma longa, the scientific name for turmeric, is a perennial plant in the Zingiberaceae family. It is most known for its rhizomes, which contain curcuminoid, the main active ingredient. Differentiuloylmethane, desmetoxycurcumin, and bisdesmetoxycurcumin are the three members of the curcuminoids group of naturally occurring polyphenol compounds. Differentiruloylmethane is the primary curcuminoid among them. Turmeric gets its characteristic yellow hue from these compounds. Carbohydrates, proteins, resins, and the three main volatile oils make up turmeric. Each of these compounds possesses pharmacological qualities. The main biologically active ingredient, curcumin, is generally known to be safe and non-toxic. Its anti-inflammatory and antioxidant qualities are what give it therapeutic benefits. However, the molecule presents a major challenge due to its low intestinal absorption, rapid metabolism-induced breakdown, and rapid excretion. It may be possible to fix this problem by developing new derivatives.[83,84]

Studies on curcumin's anti-tumor effects, particularly in breast cancer, have shown a variety of molecular targets and mechanisms of action. It has been shown that curcumin can inhibit cell division, cause programmed cell death, and induce a G2/M phase cell cycle arrest. Furthermore, curcumin controls a number of transcription factors and protein kinases, including NF-κB, Nrf2, Notch-1, and STAT3, that are involved in cell signalling pathways.[85,86]

By blocking NF-κB signalling, which controls the manifestation of cytokines and proteins essential for cell growth, survival, and metastasis, curcumin reduces inflammation. Moreover, curcumin hinders fast proliferation of breast cancer cells and initiates programmed cell death through controlling the activity of microRNAs involved in cell growth and specialization.[87,88]

Figure 4. Curcuma longa

Curcuma longa Interaction with Anti-Cancer Drugs

In breast cancer cells, the combination of curcumin and anti-cancer drugs such doxorubicin, 5-fluorouracil, docetaxel, and paclitaxel has demonstrated synergistic effects. Combination therapy has proven to be successful in increasing cell death, inhibiting cell proliferation, and overcoming drug resistance. Curcumin regulates the production of essential proteins and enzymes involved in drug metabolism and resistance. [89,90]

In summary, curcumin targets certain signalling pathways and molecular mechanisms that are critical for cell proliferation, survival, and metastasis in breast cancer. This allows curcumin to exhibit both chemo-preventative and therapeutic properties. While a substance's limited bioavailability can provide challenges, new delivery technologies such as liposomes and nanoparticles offer potential solutions to enhance a substance's therapeutic potential and effectiveness in the treatment of breast cancer.[91,92]

Green tea

Green tea is derived from the foliage and flower buds of the Camellia sinensis plant. The substance includes bioactive polyphenols. Green tea contains a group of flavonoids known as catechins, which make up a significant portion of its dry weight. Epigallocatechin-3-gallate (EGCG) is the predominant and biologically potent catechin among them. Green tea contains additional catechins such as ECG, EC, and EGC. Green tea is rich in flavones and flavonols such as apigenin, quercetin, kaempferol, and mycricetin. It also contains amino acids, carbs, minerals, trace elements, vitamins, and alkaloids like caffeine.[93,94]

Evidence indicates that the ingestion of green tea may reduce the likelihood of developing some types of cancer. The presence of antioxidants, anti-mutagenic characteristics, and chemo-preventative actions in green tea are believed to be the reasons for this. Epigallocatechin-3-gallate is generally acknowledged for its contribution to the efficacy of green tea in the prevention of cancer.

Further investigation has explored the correlation between consuming green tea and the probability of acquiring breast cancer.[95,96] Research involving large groups of women has shown that consistent use of green tea may possess the capacity to decrease likelihood of developing breast cancer. An investigation involving a substantial number of more than 45,000 females demonstrated a connection between the consumption of five or more drinks of green tea weekly and a reduced probability of developing breast cancer. Research conducted in Southeast Asia revealed that regular consumption of dehydrated green tea leaves exhibited a preventive impact on breast cancer. An extensive investigation carried out on a substantial cohort of breast cancer patients revealed a direct relationship between consistent intake of green tea and enhanced rates. The impact was especially significant in female patients who had normal cholesterol levels.[97,98]

Overall, study data from both preclinical and clinical studies suggest that green tea, particularly its main component EGCG, may have the ability to provide chemo-preventative advantages in connection to breast cancer. Regular use of green tea has the ability to decrease the likelihood of acquiring breast cancer and improve the results for persons who have already been diagnosed with the disease.[99,100]

Figure 5. Green tea leaves

The effects of using epigallocatechin-3-gallate in conjunction with anti-cancer drugs

Because of the high antioxidant and anti-cancer effects of green tea and EGCG, research has looked into the possible synergistic interaction of these substances with chemotherapy drugs. 5-aza-2-deoxycytidine is a substance that functions as a demethylating agent to increase breast cancer cells' susceptibility to anti-cancer drugs. Moreover, this combination showed a decrease in the demethylating agent's toxicity. This is accomplished by controlling the expression of PTEN and p27, two tumor suppressors, as well as miR-221/222.[101,102] Furthermore, EGCG and sunitinib co-administration resulted in a greater reduction of tumors in breast cancer cell lines than did the medication alone. By blocking the IRS/MAPK signalling pathway, which EGCG triggered, this effect was attained. Research indicates that EGCG exhibits a synergistic interaction with anti-cancer medications, suggesting potential benefits for the management of breast cancer.

Overall, studies on living things as well as in lab settings have demonstrated green tea's ability to fight cancer. Moreover, it has been discovered to supplement conventional chemotherapy medications, augmenting their efficacy. Regulating several intracellular signalling pathways is a key aspect of how it works. A chemical found in green tea called epigallocatechin-3-gallate is essential for stimulating apoptosis, a critical step in the prevention of breast cancer. Green tea's protective qualities, including those of its polyphenols and other constituents, particularly in premenopausal women. However, there is conflicting evidence from epidemiological research about green tea's possible effect on a person's risk of developing breast cancer.[103,104]

Plant echinacea

Echinacea species and bioactive compounds

Traditional botanical and therapeutic plant Echinacea belongs in the Asteraceae family. Three of nine Echinacea species are used as phototherapeutics. The three species' roots, rhizomes, and Echinacea purpurea flowers are used medicinally. These components are in 80% of commercial Echinacea. The chemical components of Echinacea were isolated using high-pressure liquid chromatography. Flavonoids-rich echinacea is a popular herbal supplement. Its therapeutic properties include decreasing inflammation, antioxidants, and immune system stimulation.[105,106]

Figure 6. Echinacea

Echinacea and medication interactions.

Cancer patients often take echinacea. 318 people were included in a study, 21% voted it the best herbal treatment. Few research have examined Echinacea in breast cancer patients. According to research, breast cancer survivors who used Echinacea, ginkgo biloba, and herbal teas had lower physical component ratings in health-related quality of life. The Black Women's Health Study found that breast cancer survivors use herbs like Echinacea more and may affect adjuvant drugs.

Echinacea was tested for anti-tumor activity in vitro. The study found that Echinacea purpurea extracts strongly inhibited BT-549 murine breast cancer cell multiplication. Furthermore, Echinacea purpurea had a stronger effect than Pallida. It discovered in Echinacea Pallida roots, inhibited MCF-7 breast cancer cell proliferation in a subsequent investigation. The liver enzyme CYP3A4 substantially processes the medication. Because Echinacea purpurea and Echinacea Pallida stimulate this enzyme, this anti-cancer therapy may be less effective, have lower plasma levels, and be ineffective. Huntimer and colleagues observed that Echinacea angustifolia roots, including the ethyl acetate fraction, chicoric acid, and doxorubicin, enhanced MCF-7 breast cancer cell growth. Interference may impair anti-cancer medication effectiveness. Echinacea purpurea hexane fractions reduced MCF-7 breast cancer cell proliferation in lab research. Cynarin from Echinacea angustifolia roots also inhibited proliferation. Echinacea and doxorubicin may interact, therefore monitor the former. A non-interacting dose of Echinacea purpurea extract with docetaxel has been documented, as has a Goey and colleagues' proposed timing. As a herbal medicine, echinacea is becoming more popular, and breast cancer patients have used it. In lab and human contexts, this drug inhibits cytochrome P450 enzymes, limiting its therapy efficacy.[107,108]

Arctium (burdock)

Burdock Bioactives

Arctium species, or burdock, are herbaceous perennials that grow near streams and roadsides. Hairy leaves and long, robust stems and roots. Three of the 18 Arctium species are prevalent in central and eastern Europe. Smaller, bigger, and woolly burdocks are Arctium minus, lappa, and tomentosum. Chinese and other cultures use arctium lappa as medication. Traditional Brazilian medicine uses its leaves as an anti-inflammatory to treat gastrointestinal issues, whereas Europe uses its roots to treat blood and dermatological issues. Asian countries treat diabetes with fruits and roots. [109,110] Numerous studies have shown that arctigenin can modulate the immune system, reduce inflammation, and fight cancer. Traditional medicine uses arctigenin. Arctigenin's anticancer efficacy has garnered interest, especially in in vitro study using lung, stomach, intestinal, ovarian, and breast cancer cell lines. Arctium lappa's anticancer capabilities have mostly been studied in vitro with human cell lines. While arctigenin did not kill breast cancer cells, it did inhibit their metastasis. Arctigenin inhibited metastasis-related heparanase and matrix metallo-proteinases. [111,112]

Figure 7. Arctium

Arctium Lappa's Effect In combination with anti-cancer drugs

Doxorubicin is a commonly used chemotherapy drug for breast cancer, but its effectiveness is limited by dose-dependent cardiotoxicity. Ghafari et al. explored the potential of Arctium lappa, or burdock root extract, in combination with doxorubicin against breast cancer cells. They found that Arctium lappa extract, like doxorubicin, reduced cell viability and induced apoptosis in breast cancer cells in a dose- and time-dependent manner. Another study showed that arctigenin, a compound found in Arctium lappa, inhibited the proliferation and induced apoptosis in triple-negative breast cancer cells by downregulating. Additionally, arctigenin enhanced the cytotoxicity of taxotere in triple-negative breast cancer cells.[113,114]

Flaxseed

Bioactive Flaxseed Ingredients

Linseed grows across the world. Flaxseed, one of the first crops, comes in brown and yellow (or golden) kinds with the same nutrients and short-chain omega-3 fatty acids. Lignans, soluble polysaccharides, dietary fibers, minerals including calcium, phosphorus, and magnesium, proteins such glutelin and globulins (linin and conlinin), and vitamins A, C, and E are present. Flaxseed has 80–20%.

Flaxseed contains significantly higher levels of lignans compared to other plants, with 800 times more lignans. These phytoestrogens are mostly secoisolariciresinol diglucoside (SDG), which makes up 95% of lignin. Alpha-linolenic acid (omega-3) is the main fatty acid in flaxseed oil, which also contains oleic, stearic, palmitic, and linoleic acids. 73% of flaxseed oil lipids are polyunsaturated, 18% monounsaturated, and 9% saturated. Soluble and insoluble fiber, antioxidants, and estrogenic lignans are abundant in flaxseed. It may also be healthy. Alpha-linolenic acid metabolism creates DHA and EPA. Omega-3s can help with atherosclerosis, hypertension, diabetes, neurological problems, and cardiovascular disease. Flaxseed and its lignan, enterolactone, suppressed breast cancer cell angiogenesis and estrogen-induced proliferation in mice. Flaxseed and its lignans inhibited vascular endothelial growth factor, a potent angiogenesis inducer, confirming in vitro observations. However, flaxseed lignan secoisolariciresinol diglucoside did not promote apoptosis or reduce breast tumor growth in athymic mice.[115,116]

Figure 8. Flaxseed

Anti-Cancer Drugs and Flaxseed

Tamoxifen adjuvantly treats metastatic ER-positive breast cancer. Since tamoxifen can cause hot flashes, many breast cancer patients prefer phytoestrogen-rich foods like soy and flaxseed to lessen symptoms and improve treatment efficacy. Flaxseed may increase or decrease tamoxifen, according to research. Flaxseed boosts tamoxifen's tumor-inhibiting actions at high and low E2. Tamoxifen and 10% flaxseed administered to athymic mice over time reduced tumor size by 55% by triggering apoptosis and restricting cell growth. Saggar et al. observed that flaxseed oil and secoisolariciresinol diglucoside reduce growth factor and estrogen receptor signaling pathway gene and protein expression in tamoxifen-treated cancers. Trastuzumab with flaxseed oil (BT-474) reduced MAPK and Akt protein phosphorylation, which slowed HER2-overexpressing tumor development.[117,118]

CONCLUSION

This review outlines the chemo-preventative and chemo-therapeutic qualities of nine herbs for breast cancer. These herbs have shown potential anti-cancer properties in living organisms and in a controlled environment by inhibiting tumor growth and cell survival mechanisms. The active compounds found in herbs control intracellular signalling regulators that are essential for the initiation and advancement of breast cancer. Due to its low absorption and pharmacokinetic properties, curcumin and thymoquinone have limited therapeutic efficacy, whereas echinacea inhibits cytochrome P450 enzymes. These limitations can be surpassed by liposome carriers and formulations based on nanotechnology, which makes oral delivery feasible.

Some herbs have anti-cancer qualities that can be increased by taking them along with common chemotherapy drugs. The drugs used in chemotherapy also got less harmful and more effective. To improve the chemo-preventive and chemotherapeutic effects of nano-curcumin formulations, take into account the synergistic effects of co-delivering these medications. To ascertain the risk-benefit analysis of co-administering the active chemical's nano-formulation with conventional chemotherapy medications, extensive clinical trials are required.

These herbs have significant chemopreventive effects. Although these herbs have various anti-cancer benefits, caution should be exercised until further clinical studies can confirm their effectiveness. Future studies on the physiologically active ingredients in these herbs should concentrate on pharmacodynamics and pharmacokinetics, safety, toxicity, and quality control. The medical benefits of these herbs need to be confirmed by more cohort studies and clinical trials.

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