

RESEARCH ARTICLE

Breast cancer. The role of herbal medication

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Abstract

For centuries, herbs and plants have been used for medicinal purposes and as food as well. This review concerns about different types of plants that retain the immune stimulating and anti-tumor properties. Large variety of active phytochemicals such as carotenoids, flavonoids, ligands, polyphenolics, terpenoids, sulfides, lignans and plant sterols has been identified in different types of herbs. Different modes of action are used by these phytochemicals. They either activate a defensive enzyme, such as glutathione transferase, or they stop cells from proliferating. The biochemical properties of *Allium sativum*, *Echinacea*, *Curcuma longa*, *Arctium lappa*, *Camellia sinensis*, *Panax ginseng*, and Flax seed were the focus of this study. *Withania somnifera*, *Amoora rohituka*, *Dysoxylum binectariferum*, and *Vaccinium macrocarpon* extracts and juices are also used as anti-breast cancer remedies. These herbs and plants' volatile oils and extracts hinder the synthesis of mevalonate, which reduces tumour growth and cholesterol synthesis.

Keywords: Anti-tumor, phytochemicals, cholesterol synthesis

Introduction

Breast cancer is the second leading cause of death worldwide. In the United Kingdom, about one in nine women will develop this disease during her lifetime. Sex, nutrition, alcohol consumption, body activity, family history, lifestyle, and endocrine elements, both exogenous and endogenous, are all linked to breast tumours. Other critical factors that contribute to breast cancer include past benign conditions and mammographic density. However, it is still unclear which factor plays the most important role in the pathogenesis of breast cancer. As a result, breast cancer has been the second leading cause of death in women. Plant-derived chemotherapeutic agents, such as fruits, leaves, bulbs, lichens, and fungi, are used to cure the disease. The botanical term "herb" refers to plants that produce fruits, seeds, and have nonwoody stems. This plants and herbs have played a critical role in human health maintenance. Herbal treatments are more common today than prescription drugs because they contain natural active compounds that can benefit human health (Anim et al. 2005).

The National Institute of Health established an office of alternative medicine in 1993 to assist qualified investigators who wish to research unconventional therapy in a systematic manner. According to a survey conducted by Eisenberg in 1993, more than one out of every three Americans used nonconventional therapy at least once a year. People want a

cure that doesn't have any negative side effects like fear, stress, insomnia, or headaches. Self-prescription herbal medicines are used to treat chronic ailments such as flu, infections, fatigue, colds, cough, anxiety, inflammation, premenstrual syndrome, depression, and cancer. Ginko, goldenseal, ginseng, garlic, Echinacea, aloe vera, and saw palmetto are some examples of plants used to treat breast cancer (Ozer et al. 2000). Many wild plants, such as black cohosh, goldenseal, ragweed, and snakeroot, are used by American Indians for medicinal purposes. Herbs, such as culinary herbs, contain aromatic ingredients and essential oils that give food flavour. The aim of this analysis is to classify the plants and extracts that may be used in the treatment of breast tumours in Pakistan and other countries. The literature was used to gather evidence on the life of plants, their scientific names, active principals, and origin.

Breast Cancer

Cancer is characterised as the abnormal division of cells in our bodies, which leads to death. Cancer cells kill healthy cells in the body. Unevenness in the body can cause cancer, and can be cured by reducing the disparity. Hundreds of billions of dollars have been invested on research to figure out what cancer is. Millions of people die as a result of cancer. According to the American Cancer Society, cancer is responsible for 2%–3% of annual deaths worldwide (Damery et al. 2011). As a result,

almost 3500 million people die each year from cancer around the world. There are several alternative options available, such as chemotherapeutics, but they are resistant to use and have many side effects. Breast cancer affects more than one million people worldwide per year. Breast cancer is commonly detected at late stages due to the lack of access to mammography for regular screening; as a result, patients receive limited and inadequate treatment, pain relief, and comfort care. Breast cancer has a significant impact on culture and women's quality of life; as a result, it has become a life-threatening disease associated with premature mortality and decreased productivity.

In advanced countries, the overall mortality rate for breast cancer is 73 percent, while in developing countries it is 57 percent. Breast cancer rates have decreased in developing countries as a result of early diagnosis and screening. As a result, three approaches to breast cancer prevention exist: clinical and general awareness, experience, and behaviours. In undeveloped countries, these methods are more widely accessible than in developing countries (Shareef et al. 2016). Measures to eliminate breast cancer at the screening level may provide an overall advantage in terms of both costs and longevity. Clinical Breast Examination is a procedure for detecting breast tumours in the general interest, as shown by research. It is simple to implement, cost-effective, and healthcare providers may openly qualify it. As a result of shifting associates of conceptive and nourishment-related causes over time, women are increasingly at risk of breast tumour, with incidence rates rising in many countries and regions around the world in recent decades. The fastest progress is seen in developing countries, where the risk of breast tumour growth has been shown to be minimal compared to developed countries. Anxiety, asthma, colds, coughs, constipation, fever, fatigue, pneumonia, insomnia, digestive disorders, premenstrual syndrome, depression, ulcers, and exhaustion are among the more prevalent conditions for which herbal medicines are prescribed today. Echinacea, ginger, ginseng, goldenseal, ginkgo, saw palmetto, aloe vera, and feverfew are some of the most commonly used herbs today.

Each breast is divided into 15–20 lobes, which are further subdivided into lobules. The lobes and lobules are connected by small “ducts”. As a result, ductal cancer is the most common form of breast cancer. As contrast to other kinds of cells, a ductal tumour develops in ductal cells and invades both breasts. Invasive and non-invasive breast cancers are two other types of breast cancer (Marchbanks et al. 2002). Non-invasive cancer is a form of tumour that does not spread beyond the area where it first appeared. Invasive breast cancer is a form of metastasize cancer that has a proclivity for spreading to tissues outside of the original site of origin. The term “general breast inflammation” refers to a less serious form of tumour known as an “interstitial breast tumour.” Other types of breast cancer include medullary cancer, which is characterised as “an intrusive breast tumour that produces a distinct boundary between cancerous and normal tissue,” mucinous cancer, which is caused by tumour cells that create mucus, and tube-like cancer.

Any woman is at risk of contracting breast cancer. For quite some time, a few relatively strong risk factors for breast cancer that affect large swaths of the population have been identified.

However, the majority of breast tumour cases occur in women who have no known risk factors other than their sex (Lambert et al. 2003). Female sex, old age, previous breast tumour, a form of breast infection, hereditary components, early age at menarche, menopause at old age, old age at first full-term birth, stoutness after menopause, low body activity, race/origin, and high-measurements presentation to radiotherapy in life are the “well-known” risk elements for breast tumour. Never having become pregnant, having only one pregnancy rather than many, not breastfeeding after pregnancy, using postmenopausal oestrogen substitution therapy or postmenopausal hormone substitution therapy, orally taking contraceptives, and certain specific dietary habits such as a high fat intake and low fibre intake, are both “estimated” risk factors for breast cancer. Regardless of the fact that men can and do develop breast tumours, a woman is 100 times more likely than a male to develop the disease.

Since women have more breast tissue than men, they are at a greater risk of developing a tumour. Furthermore, oestrogen helps to improve the development of breast tumours. Breast cancer is more common in middle-aged women. This risk increases as a woman's age rises, particularly after the age of 40 (Freudenheim et al. 1996). In the United States, women above the age of 50 account for more than three-quarters of all breast tumours. Breast tumour risk is higher in women who have close blood relatives (mother, sister, or girl) who have had the disease. The chance of expansion is greater if any ancestors acquired a breast tumour by the age of 50, or in both breasts. Nonetheless, the majority of women who experience breast cancer (around 80%) have no family history of the disease. Hereditary factors are thought to play a role in the effect of family history on breast cancer risk. Approximately 5%-10% of all breast growth cases may be attributed to specific acquired single-quality transformations, and several separate cases have an inherited component. The evidence from particular families where breast growth occurs often and from large epidemiological research has shown that a few women have a maternal tendency to breast growth. Hereditary breast tumours are inherited in an autosomal dominated way in some families. Hereditary breast cancer spreads due to germ line mutations in the BRCA1 and BRCA2 genes, which causes cancer to propagate. This genetic cancer is diagnosed using autopsy findings and histopathological results. Aside from mutations in the BRCA1 and BRCA2 genes, there are some unexplained genetic abnormalities that place people at risk for breast cancer. Women who reach menarche at the age of 12 or younger, and those who reach menopause at the age of 55, have a higher risk of breast cancer than other women. This connection is due to the development of oestrogen. During the reproductive years, women's bodies contain a lot of oestrogen (Donaldson et al. 2004).

Women that start bleeding at a younger age and/or reach menopause later in life are exposed to higher levels of oestrogen for a longer period of time than women who experience a late menarche or early menopause. The age of the woman at the time of her first birth is another aspect of her conception experience that is linked to the risk of breast development. Women who have their first full-term baby at a relatively early age have a lower risk of breast cancer than women who never

have children or who have their first child later in life. Obesity has been consistently linked to a higher risk of breast tumour development in postmenopausal women. Estrogen generation can interfere in this relationship a second time. Fat cells produce oestrogen, and stout postmenopausal women have higher oestrogen levels in their blood than slim women. According to research, premenopausal women who are physically involved have a lower risk of breast tumour development than women who are not. Body activity during puberty can be especially protective, and its effect may be strongest in women who have had at least one full-term pregnancy. Non-Hispanic white, Hawaiian, and dark women have the highest breast tumour growth risk, according to studies.

Women that were exposed to heavy levels of radiation during puberty had a higher risk of breast cancer. This connection was discovered among both atomic bomb survivors and women who received heavy doses of radiation as part of their treatment. Other endogenous hormonal causes, such as a woman's age at her first pregnancy and when she has a new-born, have an impact on breast cancer. Breast cancer is more likely to occur in women who have never had a child. If the first pregnancy happens after the age of 30–35, the chance of breast cancer is reduced. Long-term use of postmenopausal oestrogen therapy or combined oestrogen/progestin hormone replacement therapy can be linked to an increased risk of breast cancer (Chen et al. 2002).

The connection between the use of oral contraceptives and the development of breast cancer has been studied. Oral contraceptives have been linked to increased breast tumour development in a number of tests, but the results have been mixed. In either case, these studies have shown that oral contraceptives have little effect on the risk of breast tumour development. Breast tumour factor can be linked to the use of postmenopausal hormone therapy, either alone or in tandem with other therapies. It was also discovered that there is a connection between oral contraceptive use and breast cancer, despite the fact that oral contraceptives do not have a long-term impact on breast cancer. According to research, there is a connection between breast cancer and diet, with low rates of disease in Asia and high rates in Western industrialised nations. Between vegetarians and non-vegetarians, an inclusive finding was discovered (Shareef et al. 2016). A link was found in alcohol, cigarette smoking and breast tumor. Breast cancer spreads more quickly in women who have already been diagnosed with a tumour in the breast. Premature abortion and incomplete pregnancies have been attributed to an increased risk of breast cancer. Breast cancer is caused by a high oestrogen level during an incomplete pregnancy.

Traditional herbs used for the prevention of breast cancer around the world

Breast cancer is a condition that should be avoided. Estrogens play an important function in the proliferation of both normal and neoplastic breast epithelial cells. Estrogen receptor positive breast cancer accounts for almost 40%-70% of all breast cancers. As a result, one of the important ways for the detection and chemoprevention of breast cancer is to block the oestrogen receptor. Phytoestrogens, or estrogen-like compounds found in plants, were first proposed as cancer-

preventive agents. An epidemiological analysis found a low incidence of breast cancer in the soy-consuming community, substantiating this argument. Flavones, flavanones, lignans, coumestans, and stilbenes are the structural groups of phytoestrogen. Isoflavones are abundant in soybeans and soy products. Legumes and lignans, which can be present in beans, nuts, whole grains, berries, and vegetables, are two other phytoestrogen groups. The incidence of breast cancer in the United States has historically been 4-7 times higher than in Asian populations, where dietary isoflavone intake is comparatively as high as 20 mg/d to 80 mg/d. Furthermore, epidemiological findings showed an insignificant 30% decrease in breast cancer risk for women who consumed a higher percentage of dietary lignan. As a result, eating a phytoestrogen-rich diet is one of the many possible breast cancer-prevention lifestyles. Recent data suggests that phytoestrogen production prevents the function of essential steroidogenic enzymes involved in the production of estradiol from circulating androgens and oestrogen sulphate. As a result, this practise can play a key role in breast cancer prevention. Phytoestrogens have also been confirmed to stimulate the G-protein coupled receptor, GPR30 or GPER-1, which has been identified as a novel oestrogen receptor and plays a key role in estrogen-dependent diseases including breast cancer (Qi et al. 2010). The function of phytoestrogens, on the other hand, is unknown and is dependent on a number of factors, including their composition, metabolism, and relative abundance compared to endogenous oestrogen. Phenolic acids, flavonoids, tannins, quinones, anthocyanins, and other naturally occurring phenolic compounds play an important role in cancer prevention and/or treatment. These phenolic compounds are found in medicinal herbs and dietary plants in abundance. By virtue of their wide variety of biological activities, some phenolic compounds contribute to the inhibition of carcinogenesis mechanisms and exhibit chemopreventive properties.

Traditional herbs used for the treatment of breast cancer around the world

Plants have played an important role in human survival and development since they have supported fundamental human needs such as food, clothes, shelter, and medicine since the dawn of time. Plants are the foundation of western medicine systems such as Ayurveda, Unani, and Chinese traditional medicine, which have fulfilled humanity's health needs for thousands of years. Herbal medicine is used by a considerable portion of the population of developing and underdeveloped countries to cure their primary health problems. Traditional herbal remedies have grown in popularity as a result of their low cost, abundance, and lack of side effects. In recent years, there has been a greater emphasis on plant science around the world in order to discover drug-like compounds from commonly used medicinal plants. Furthermore, some naturally occurring plant-based compounds such as curcumin, resveratrol, quercetin, and others have shown positive anti-cancer effects and are gaining popularity as a chemotherapeutic adjuvant. Furthermore, naturally occurring chemicals are less harmful to healthy cells and exhibit selective toxicity against dysfunctional or diseased cells in some circumstances. This may explain why a vast percentage of products on the market currently have structures that are structurally identical to those found in

nature. Herbal compounds include a wide range of anticancer properties, including antioxidant, anti-inflammatory, antimutagenic, and apoptosis-inducing properties, which can aid deter cancer from developing in the first place (Shareef et al. 2016; Marchbanks et al. 2016; Lambert et al. 2003). By cell cycle arrest, induction of apoptosis, controlling carcinogen metabolism and oncogenic expression, inhibiting cell adhesion, proliferation, and migration, and blocking signalling pathways that are important for cancer progression, dietary consumption of adequate amounts of these herbal products can aid in the prevention and treatment of breast cancer. Between 1981 and 2014, 136 anticancer drugs were approved around the world, with herbal compounds or derivatives accounting for nearly 83 percent of them. Vincristine, vinblastine, paclitaxel, and docetaxel are among the anticancer medications currently being used to cure breast cancer. Despite herbal products' effectiveness in treating breast cancer and its complications, few herbal products make it to preclinical or clinical trials. As a result, further work would be required to effectively move these agents to an appropriate therapeutic environment in order to determine their herbal therapy ability.

Chinese Medication

In conventional medicinal systems, natural drugs are used regularly to deal with the signs and symptoms related to most cancers and the facet consequences of most cancers remedy (Lambert et al. 2003; Freudenheim et al. 1996; Donaldson et al. 2004). Herbal formulations utilized in TCM consist of combos of natural compounds constituted as decoctions, tea, injections, or capsules, which might be speculated to own anticancer compounds and are used by myself or as adjuvants to current chemotherapy regimens to enhance efficacy and/or lessen drug-precipitated toxicity. Although TCM is generally used to counteract the facet consequences of chemotherapy, medical proof for its use in girls with breast most cancers nonetheless is being collected. Among the maximum not unusualplace Chinese medicinal herb formulations utilized in preclinical and scientific exercise for breast most cancers remedy are Danggui (*Angelica sinensis-radix*) and Ren Shen (*Panax ginseng-radix*), which might be stated to have capability useful synergistic consequences that consist of reducing remedy-related toxicity, psychosocial stress, and fatigue. Jia-wei-xiao-yao-san, commercially regarded as "Augmented Rambling Powder," a Chinese medicinal herb system containing Danggui, is the maximum often prescribed components for treating breast most cancers and chemotherapy-associated signs and symptoms *via* way of means of TCM practitioners in Taiwan. This system has a protracted records of use for comfort of blood toxicity and sleep disturbance. It is likewise used to alleviate warm flushes and decrease serum degrees of inflammatory cytokines, IL-6, IL-8, and macrophage protein 1- .

LSC101, an encapsulated homogenized combination of dry powdered extracts from a mixture of medicinal herbs, including *Astragalus membranaceus*, *Poriae cocos*, *Atractylodes macrocephala*, *Lycium chinense*, *Ligustrum lucidum*, *Paeonia lactiflora*, *Paeonia obovata*, *Citrus reticulata*, *Ophiopogon japonicus*, *Milletia reticulata*, *Oldenlandia diffusa*, *Scutellaria barbata*, *Prunella vulgaris*, and *Glehnia littoralis*, is used broadly through breast most cancers sufferers. Its efficacy in attenuating the

hematological headaches of chemotherapy has been examined in clinical settings (Ho et al. 2002). In mouse breast most cancers models, using LSC101 collectively with doxorubicin led to noticeably better neutrophil, splenic erythrocyte, and leukocyte counts. In addition, using LSC101 collectively with traditional chemotherapy regimens furnished safety in opposition to slight to slight chemotherapy-caused anemia and neutropenia, helping its use for lowering hematological toxicity however now no longer most cancers prevention. Though it isn't but clean how the compounds in LSC101 lessen hematological toxicity, it's far suspected that the interactions and synergistic results of the energetic compounds from the mixture of herbs can be chargeable for the reported efficacy. Some of the factor herbs, for example, *Ophiopogon japonicus* and *Astragalus membranaceus*, in LSC101 were independently proven to stimulate the manufacturing of erythroid progenitor cells in mice and sell restoration of hematopoietic feature in sufferers with continual aplastic anemia. A TCM method composed of 5 herbs, usually acknowledged as "Ruyiping" and "Runing II" is used as remedy for detoxing and stopping relapse, recurrence, and metastasis in breast most cancers sufferers after mastectomy. Clinical proof shows that the mechanism of motion of this natural method is through inhibition of angiogenesis and downregulation of Vascular Endothelial Boom Factor (VEGF) and VEGF receptor in addition to Micro-Vessel Count (MVC) and Micro-Vessel Area (MVA).

Shenqi Fuzheng Injection (SFI), a TCM formula utilized in repairing immune feature on the mobile and molecular ranges, is likewise powerful in assuaging myelosuppression and GI tract response triggered with the aid of using chemotherapy and surgical operation. In scientific evaluations, the protein expressions of CD83, CD80, and CD86 in sufferers' tumor tissue and auxiliary lymph nodes have been detected earlier than and after remedy. Results advocate that SFI should assist restore immunity impaired with the aid of using most cancers and most cancers remedy with the aid of using activating dendritic cells and upregulating costimulatory molecules (Treasure 2005). Clinical research the use of a herbal nutritional complement composed of an aggregate of medicinal mushrooms *Coriolus versicolor*, *Ganoderma lucidum*, and *Phellinus linteus* and medicinal herbs *Scutellaria barbata*, *Astragalus membranaceus*, and *Curcuma longa* recommended that the components can alleviate chemotherapy-triggered toxicity in liver, spleen, kidney, lung, and coronary heart tissue. *In vitro* research additionally elucidated the mechanism of movement of this mushroom-natural formula in inhibiting proliferation and reducing the invasive conduct of a rather metastatic human most cancers cellular line, MDA-MB-231, with the aid of using the inhibition of cyclin A1 expression and with the aid of using the downregulation of CXCR4.

A aggregate of rose geranium (*Pelargonium graveolens*, Geraniaceae), *Ganoderma tsugae* (Ganodermataceae), *Codonopsis pilosula* (Campanulaceae), and *Angelica sinensis* (Apiaceae) (RG-CMH) has been utilized in TCM remedies for breast most cancers and is related to immunomodulation primarily based totally on anti-inflammatory and wound-restoration houses attributed to the synergistic interest of the additives of the herbs. In one RCT, RG-CHM intervention stepped forward the immune cellular remember of most cancers sufferers receiving

chemotherapy and/or radiotherapy stopping leukopenia and immune impairment related to a lower in ranges of T cells, helper T cells, cytotoxic T cells, and herbal killer cells in comparison with the institution receiving placebo remedy. However, the variations among the 2 companies have been now no longer statistically significant. The effects did show, however, that the management of RG-CMH to sufferers receiving chemotherapy/radiotherapy behind schedule the discount in ranges of leucocytes and neutrophils skilled with the aid of using sufferers present process most cancers remedy.

Yunzhi-Danshen (*Coriolus versicolor* and *Salvia miltiorrhiza*) pills had been proven to advantage the circulatory machine thru vasodilation, immunomodulation, and antidementia activities. Results of a latest RCT confirmed that absolutely the counts of T-helper lymphocytes (CD4⁺), the ratio of T-helper (CD4⁺)/T suppressor and cytotoxic lymphocytes (CD8⁺), and the share and absolutely the counts of B lymphocytes have been extensively multiplied in sufferers after taking Yunzhi-Danshen pills. These scientific findings mean that ordinary oral intake of Yunzhi-Danshen pills might be useful for selling immunological feature in breast most cancers sufferers after chemotherapy (Richardson 2001). These findings have been additionally supported with the aid of using *in vitro* effects displaying that Yunzhi-Danshen remedy inhibited most cancers cellular proliferation with the aid of using cellular-cycle arrest and downregulation of Akt phosphorylation in MCF7 cells, a human breast most cancers cellular line, and with the aid of using inducing apoptosis.

A few natural\herbal products used in treatment are listed below:

Garlic: Garlic (*Allium sativum*) has been used to cure a variety of ailments for hundreds of years. It includes a hundred or so therapeutically beneficial secondary metabolites, such as alliin, alliinase, and allicin, to name a few. Garlic oil contains alliin, an amino acid that is converted to allicin after the rhizomes are crumpled. Allicin, which is responsible for odour and medicinal properties, is an originator of sulfur-containing compounds. Ajoene, a sulfur-binding compound used in garlic oil, is another sulfur-binding substance. While selenium acts as an antioxidant, ajoene slows the progression of cancer. Garlic also contains bioflavonoids such as cyanidin and quercetin, which have antioxidant effects. Garlic's anti-cancer properties are due to the high content of organic sulphides and polysulfides (Wheat and Currie 2008). The mechanism behind anti-tumor activity promoting lymphocytes and macrophages is that they destroy cancerous cells and disrupt the metabolism of tumour cells.

Echinacea: *Echinacea* is a member of the *Asteraceae* family. It is an uninhabited aromatic plant that grows mostly in North America's Great Plains and eastern areas, as well as in Europe. *Echinacea purpurea*, *Echinacea angustifolia*, and *Echinacea pallida* are the three most widespread plants used in herbal remedies. However, *E. purpurea* is the most widely used species for study and care. Purple coneflower, Kansas snakeroot, and black Sampson are several common names associated with *Echinacea*. Researchers discovered that *E. purpurea* increases the number of natural killer cells in mice under study. In the future, *E. purpurea* may be used as an anti-cancer treatment. *Echinacea* contains

flavonoids, which serve as immune stimulants. Flavonoids stimulate lymphocyte activity, which enhances macrophage phagocytosis and the action of natural killer cells, prompting interferon assembly, and it has also lessened the harmful effects of radiotherapy and chemotherapy, according to Winston et al. Flavonoids promote lymphocyte activity, which improves phagocytosis by macrophages and the action of natural killer cells, prompting interferon assembly, and it has also lessened the harmful effects of radiotherapy and chemotherapy, according to Winston. It also aids people in extending their life time as their disease progresses. Commercial preparations of Echinacea juice have been shown to increase macrophage cytokine production (Wheat and Currie 2008). T-cell and B-cell 7 activation and proliferation have less direct results. Several Echinacea components are examined to see whether they play a part in the immune system's unique sound effects.

Carotenoids: Green, herb with leaf, rose hips contain an active compound known as "carotenoids." Saffron, annatto, and paprika are examples of aromatic plants that are used as dyeing agents. Vegetable and fruit consumption has been related to less tumour growth in various ways. Dietary intake of carotenoids also lowers the risk of tumour development. The carotenoid compounds are powerful antioxidants with a wide range of therapeutic properties, including scavenging free radicals, shielding cells from oxidative damage, improving gap intersections, stimulating the immune system, and regulating enzyme function, all of which contribute to cancer development and promote the activity of the body's immune system.

Burdock: *Arctium lappa* is the scientific term for burdock. Its root can be found in Europe and Asia and is used there. Burdock is used in a variety of herbal medicines for a variety of ailments. It has a gummy feel and a soft flavour. Burdock was once used to treat arthritis, tonsillitis, and measles, but it has now been discovered that it has antitumor properties (Salaga et al. 2014). It contains active ingredients that influence oncogene shifts. Burdock has been used to cure breast cancer, ovarian cancer, bladder cancer, malignant melanoma, lymphoma, and pancreatic cancer cells. It reduces pressure, shrinks tumours, and extends the period of survival. During cancer, a large amount of nutrients is needed to survive the rapid proliferation and division of cells. Cancer cells, on the other hand, may survive under stressful environments such as low oxygen and low carbohydrates since they have a high capacity for stress. Arctigenin is an important ingredient used in burdock seeds. Arctigenin has been shown to be capable of removing tumour cells even though nutrients are scarce. Burdock root contains anti-oxidants of the flavonoid and polyphenol types, which may have an inhibitory effect on tumour development. The extract of root protects normal body cells from radioactive agents and reduces cell mutation. Tannin, a phenolic acid, is the most essential active ingredient found in burdock. It activates macrophages, prevents cancer from spreading, and maintains immune-modulatory properties (Ho et al. 2002).

Turmeric: *Curcuma longa* is the scientific word for turmeric. Turmeric gives food a dark yellow flavour. Turmeric's active ingredient, curcumin, is found in the rhizome and rootstock. Curcumin's phenolic compounds are believed to have anticancer properties. Turmeric inhibits the spread of lung,

breast, scalp, and stomach cancers. Curcumin, an antioxidant, affects the synthesis of eicosanoids including prostaglandin E-2 (PGE-2). In humans, it also has anti-inflammatory properties. Curcumin has been shown to have inhibitory effects on cancer development at all stages, including initiation, promotion, and proliferation. Turmeric inhibits the synthesis of nitrosamine, resulting in an improvement of the body's natural antioxidant activity (Barreto et al. 2000). Curcumin increases the amount of glutathione and other non-protein sulphahydryls in the body, and these sulphahydryls work directly on various enzymes.

Flax Seed: Tiny brown and golden hard-coated seeds are produced by the flax plant. All of the active ingredients are present in these tiny seeds. Flax seeds are high in dietary fibre, omega-3 fatty acids, and lignans, both of which are beneficial to your health. The metabolism of lignans to enterodiol and enterolactone, which occurs in the digestive tract, results in estrogenic development in flax seeds. Flax seeds contain more active phytoestrogens than soy products, and eating flax seeds induces a significant difference in 2-hydroxyesterone reduction relative to soy protein. Ground flax seeds have been found to have potent anti-cancer efficacy by Lilian Thompson's study group at the University of Toronto (Salaga et al. 2014). An experiment was carried out on mice in which cancer was first caused in the mice by administering carcinogens, and then anti-cancer activity of flax seed was detected in one population by combining lignin in the mice's diet. The tumour load was reduced as a result of this experiment. The malignancies were reduced by flax seeds and secoisolariciresinol diglycoside.

This research group recently used human breast cancer cells to cause tumours in mice. Although cancer spreads, mice were fed a bland diet for eight weeks after cancer cells were injected. One party was given 10% flax seeds, while the other was given a standard diet. Flax seeds reduced the rate of cancer growth by 45 percent. Flax seeds enhance the morphogenesis of mammary glands in rodents. Female mice fed a 10% flax seed diet had a higher number of terminal end buds and terminal ducts in their mammary glands, according to the researchers. Extra epithelial cell division is present. Females of both sexes have increased distinction. Females have demonstrated a low occurrence of breast tumours after being injected with carcinogens in the mammary glands. As a result, flax seeds in female offspring will improve mouse mammary tissue differentiation, prevent malignancies, and reduce tumour growth, rendering them less vulnerable to carcinogens (Gratus et al. 2009).

Green Tea: *Camellia sinensis* is the scientific name for green tea. Polyphenolic compounds are thought to have anticancer properties. *C. sinensis* contains a small volume of Epigallocatechin Gallate (EGGG), a polyphenol. Green tea has been shown to have antitumor and antimutagenic properties, according to studies. EGGG protects cells from the DNA damage caused by oxygen reactive species. Green tea polyphenols inhibit cancer cell proliferation and promote tumour cell necrosis and apoptosis, according to animal studies. Tea catechins not only activate the immune system, but they also suppress tumour cell metastasis and angiogenesis. Green tea has been found to be effective against colon and stomach cancer in several trials. Tea and its main catechins lower the chance of tumours in a variety

of body organs. Green tea can help to reduce the harmful effects of radiation. Tea's antioxidant function is responsible for all of the health benefits.

Ginseng: *Panax ginseng* is the scientific name for ginseng. It is a long-lived plant that grows mostly in China, Korea, Japan, and Russia. The dried root of this plant is included. It may be used to treat a variety of ailments, including cancer. Ginseng's active ingredients have been shown to minimise or inhibit the production of tumour necrosis factor in mouse skin, hinder the proliferation and metastases of cancerous cells, promote cell differentiation, and increase interferon levels. Some types of cancerous cells can also be hampered by the ingredients in ginseng. In addition, a study conducted in Korea concluded that ginseng decreases the risk of cancer in humans (Ohnishi and Takeda 2015). In comparison to fresh sliced ginseng, juice, or tea, the most effective and active form of ginseng for cancer prevention is its extract and dried powder. Ginseng prevents tumour growth by interfering with DNA synthesis. The active compound of *P. ginseng* has many beneficial properties, including the reactivation of natural killer cells that have been damaged by chemotherapy and radiotherapy, the induction of macrophages, and the enhancement of antibody production.

Black cohosh: *Cimicifuga racemosa* is the scientific word for black cohosh. It's a shrub that grows in North America's eastern forests. Black cohosh was most widely used for breast cancer patients during radiotherapy and chemotherapy. It has been used for decades by Native Americans to relieve menopausal symptoms, premenstrual discomfort, and dysmenorrhea. It also causes complications similar to abortion. Lydia Pinkham's Vegetable Compound was a well-known patent drug, and this herb was a key ingredient. It was also used in pharmacopoeia from the 19th century (Dass and Mathur 2009). In drug stores, you can find a wide variety of black cohosh preparations. Herbalists have shown that they are a healthy and successful treatment option for menopausal symptoms.

Females who were advised by their doctors to avoid Hormonal Replacement Therapy (HRT) have done so. The herb's effects on menopausal symptoms have been shown in the majority of tests. While the active principles of black cohosh are unknown, it is thought to include triterpene glycosides, as well as a trace amount of resins and caffeic, isoferulic, and fukinolic acids. There are some ambiguities about black cohosh's estrogenic and anti-estrogenic function. Various scientific findings have shown conflicting reports, with some claiming that it increases or decreases cancer cell development in culture. When given in conjunction with other chemotherapeutic agents, black cohosh has synergistic effects for breast cancer patients, according to the literature.

Vitamin D: Skin exposure to the sun produces vitamin D. In the summer, simple touch with palms, muscles, and face produces a large quantity of vitamin D. Standing in the sun on the beach before the skin turns pink is equivalent to a 20,000 IU vitamin D2 oral dosage. To sustain an adequate level of vitamin, our bodies only need 1000 IU per day (Da-Yong and Ting-Ren 2019). In the lack of sunlight, oral vitamin D uptake is the best way to keep the levels up. 4000 IU can be taken conveniently in one day while still providing other benefits. The kidneys are in charge of keeping the active hormonal form of vitamin

D in the blood. This active form of vitamin D has anti-cancer properties. Vital organs of the body performed their functions by converting the main circulating source of vitamin D, 25(OH) D, into the hormonal form, 1, 25(OH) 2D. Many of these organs have a local pathway for converting the circulating form into hormonal form, which is aided by exposure to sunlight.

Cytotoxic herbal cure

The selective toxicity of herbal treatments against cancer cells is one of their most intriguing characteristics. A variety of phytochemicals have been shown to have selective toxicity against breast cancer cells. One of them, artemisinin, was isolated from *Artemisia annua* L. and found to be selectively cytotoxic against breast cancer cells when a sufficient amount of iron (ferrous iron) was present in the cells. Artemisinin and its analogues can selectively kill cancer cells under high iron concentrations when cancer cells have a higher iron influx. Polyphenols from *Artemisia annua* L. (Jaradat et al. 2016) were also found to inhibit the adhesion and Epithelial-Mesenchymal Transformation (EMT) of MDA-MB-231 cells, which are extremely metastatic breast cancer cells. Aside from that, polyphenol-rich extracts of *Hibiscus sabdariffa* and aqueous extract of *Brucea javanica* have also been shown to have selective cytotoxicity against MCF7 and HTB-126 breast cancer cell lines, respectively. However, further research is needed to isolate the specific cytotoxic components of these plants.

Combination therapy by herbal remedies and synthetic drugs

Combination treatment, which combines natural therapy with synthetic medications, could be the only option for women with advanced breast cancer who are unable to undergo surgery. A herbal drug's combination effect with conventional cancer drugs can increase one of the drugs' bioavailability, making the treatment more successful. Furthermore, combining natural therapies with chemotherapy reduces the dosage of conventional treatment, resulting in reduced toxicity and side effects. Several scholars have proposed that medicinal compounds be used as a treatment modality because they improve the anticancer efficacy of currently available medications (Ezhilarasan 2018).

Herbal supplements and nutraceuticals for treatment

Cancer has been found to be a condition that can be avoided by changing one's diet and nutrition. According to a recent study, diet is linked to about 35% of cancer cases. Several epidemiological and experimental trials have shown that a healthy consumption of fruits, vegetables, and herbal products is inversely related to the prevalence of breast cancer. A diet high in phytoestrogens, polyphenols, and other chemopreventive agents lowers the risk of breast cancer. Herbal dietary supplements are less poisonous and more readily metabolised. Furthermore, in post-chemotherapy patients, nutritional intake of these herbal therapies aids in the reduction of side effects. Hot flushes are one of the most common signs of adjuvant chemotherapeutic injury in post-treatment breast cancer patients (Cohen et al. 2002). Black cohosh, also known as *Actaea racemosa*, is a common treatment for hot flushes in breast cancer patients, with mixed but positive outcomes

The molecular mechanism of herbal compounds' anticancer role in breast cancer

Anticancer properties of herbal compounds include antioxidant, cytotoxic, anti-proliferative, and apoptotic function, among others. Methyltransferase inhibitors, DNA shielding agents, antioxidants, histone deacetylase inhibitors, and mitosis disruptors are among the five types of plant-based cancer agents. Plant-derived compounds have antioxidant, cytotoxic, antimetastatic, and apoptotic activity, which both contribute to the anti-carcinogenesis process. Others aid in chemoprevention by preventing DNA damage, modulating carcinogenesis signalling, and inducing cell death by apoptosis. Several *in vitro* and *in vivo* studies back up the anticancer properties of herbal compounds (Korrapati et al. 2016).

Herbal compounds antioxidant activity

As the equilibrium between the development of reactive oxygen species and antioxidant protection is disrupted, herbal compounds of oxidative stress develop antioxidant function. The formation of oxidative stress and the subsequent production of Reactive Oxygen Species (ROS) have been related to the pathogenesis of many diseases, including cancer. The body's antioxidant system deals with oxidative stress, and some herbal compounds may aid improve this machinery. Curcumin, for example, boosts the activity of antioxidant enzymes, making cells more resistant to oxidative harm (Qi et al. 2010; Ho et al. 2002; Treasure 2005; Richardson 2001; Wheat and Currie 2008). Curcumin was also shown to increase the behaviours of GSH, SOD, GPx, GR, GST, and CAT in paracetamol-treated rats. Other plant-based compounds, such as epigallocatechin gallate, a component of green tea, were found to reduce lipid peroxidation and protein carbonyl content in rats when given orally, likely through improving GSH redox status. Similarly, some herbal compounds tend to mitigate oxidative stress and hence play a part in cancer prevention.

Anti-angiogenesis activity of herbal compounds

A range of herbal compounds can aid in the prevention of angiogenesis in breast cancer. The most active angiogenesis inhibitor is genistein, a flavonoid phytoestrogen related to decreased expression of VEGF, PDGF, uPA, and MMP-2 and MMP-9. Curcumin has also been discovered to be an important regulator of angiogenesis, reducing the expression of various proangiogenic proteins such as VEGF and essential fibroblast growth factor. Resveratrol and quercetin blocked the migration and tube development of bovine aorta endothelial cells, which inhibited angiogenesis. The angiogenesis of bovine aorta endothelial cells was inhibited by resveratrol and quercetin, which inhibited migration and tube formation. Furthermore, catechin derivatives found in green tea, such as Epicatechin (EC), Epigallocatechin (EGC), Epicatechin-3-Gallate (ECG), and Epigallocatechin-3-Gallate (EGCG), inhibits angiogenesis. Inhibition of Vascular Endothelial Growth Factor (VEGF) formation and reduction of Matrix Metalloproteinase-2 (MMP-2) activity in MDA-MB231 breast cancer cells demonstrated EGCG's anti-angiogenic activity (Jaradat et al. 2016).

Conclusion

Breast cancer is caused by a complex set of factors; many

of them function alone or in combination, particularly in high-risk individuals. It's important to understand the pathogenesis of this common condition, which is linked to high mortality and morbidity if not caught early. Early screening of high-risk patients, as well as proper monitoring in treated cases, has been advocated in order to detect recurrence at an early stage. Advances in healthcare science, on the other hand, have resulted in the discovery and classification of the majority of breast cancer varieties, as well as their subsequent cures. However, due to a variety of risk factors, the occurrence and prevalence of breast cancer is the at an alarming pace in both developed and emerging countries. Breast cancer incidences have decreased, mortality has increased, and life expectancy has improved as a result of improved synthetic medications and hormone treatment. However, long-term use of synthetic anticancer medications has been attributed to a number of health hazards or side effects as a result of the drugs' toxicity in normal cells. Herbal chemoprevention is attracting a lot of attention because it's a low-cost, easy-to-apply, acceptable, and accessible solution to cancer control and management. Herbal treatments play an important part in the treatment of breast cancer and the toxicity that comes with it. The use of natural supplements in conjunction with chemotherapy may be a cost-effective and efficient way to cure breast cancer. Adjuvant therapy has been shown to have a synergistic anticancer effect, reducing drug toxicity, suppressing drug tolerance, and providing rapid drug action, both of which improve care efficiency. Furthermore, by improving the drug's efficacy, combinatory therapy can improve the therapeutic index of the synthetic partner. Plant-derived anticancer drugs such as vinblastine, vincristine, taxols, and others have shown promising chemotherapeutic promise and are currently being used in preclinical or clinical trials for breast cancer care. A large number of phytochemicals have been discovered in the last decade that has shown promising anticancer efficacy in vivo and in vitro breast cancer models. Several compounds, such as artemisinin and isothiocyanates, demonstrated selective toxicity against cancer cells, indicating that clinical trials of these compounds are warranted. Furthermore, phytoestrogens with a high affinity for oestrogen receptors and the ability to develop functional responses across them uncovered new possibilities for hormone replacement therapy. Overall, studying the molecular mechanisms of association between herbal compounds and cancer cells in the tumoral system will aid in the development of new anticancer medicines that are less harmful and inexpensive. This illustrates the fact that these objectives can only be met if promising anticancer herbal compounds can be effectively translated to an ideal therapeutic environment for the use of herbal therapies.

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