

## EFFECTS OF HERBAL MEDICINES IN THE TREATMENT OF BREAST CANCER

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### ABSTRACT

When it comes to cancers affecting women, breast cancer ranks first and foremost. Worldwide, it ranks high as a cause of mortality for females and the second most common cancer detected. Traditional cancer treatments, such radiation and chemotherapy, have a high death rate when it comes to breast cancer. In addition, tumours that are resistant to more than one medicine pose a significant challenge to cancer treatment and account for a disproportionate share of cancer-related fatalities. A lot of research is currently focused on finding breast cancer alternative therapy systems that may be utilised as therapies, adjuvant treatments alongside existing treatments, or chemopreventive drugs in order to tackle this dangerous problem. Few herbal medications are advancing into the preclinical or clinical stages, despite their effectiveness in treating breast cancer and its complications.

**KEYWORDS:** Chemotherapy, Therapeutics, Multidrug resistant.

### INTRODUCTION

In 2010, there were estimated to be 1,383,500 newly diagnosed cases of breast cancer and 458,400 fatalities caused by the disease. It is the most frequent cancer among women and the leading cause of cancer-related deaths globally. Breast cancer ranks highest among female cancers in the US, surpassing even skin cancer.<sup>[1]</sup> On a worldwide scale, the breast cancer incidence might vary by a factor of five.<sup>[2]</sup>

Globally, breast cancer is a major issue in terms of public health<sup>[3]</sup>, It ranks high among female cancers and is a leading cause of cancer-related mortality worldwide.<sup>[4]</sup> A growing number of variables appear to be linked to an increase in the incidence of breast cancer,

which has become a deadly illness.<sup>[5]</sup> A variety of internal and external variables can amplify breast cancer's pathogenesis<sup>[6]</sup> Several other considerations, such as the potential adverse effects of standard medical treatments like chemotherapy,<sup>[7]</sup> and radiotherapy<sup>[8]</sup> are adding to the difficulty of caring for breast cancer patients and the overall load. Multidrug resistance (MDR) is a major concern with current treatment methods.<sup>[9,10]</sup> The breast cancer survival rate is so low, and this is a major reason why. Efforts are being made to develop novel breast cancer medicines, including therapeutics, adjuvant treatments (used in combination with existing treatments), and chemopreventive medications, in response to this devastating trend.<sup>[11–14]</sup> Breast cancer commonly develops and progresses through several paths.<sup>[15–18]</sup> Once again, a battery of biomarkers is utilised by the diagnostic procedure.<sup>[19]</sup> Developing an artificial molecule that mimics a naturally occurring one might be a promising new treatment option.<sup>[20]</sup> Over half of all medications have their origins in naturally occurring substances; of these, 75 percent of anticancer medications have their origins in naturally occurring substances originating from plants.<sup>[21]</sup>

### **Breast cancer survivors experiencing menopause symptoms**

After a breast cancer diagnosis, menopausal symptoms can develop for a variety of reasons. It is common practice to advise women experiencing symptoms who have been on hormones to discontinue treatment following a diagnosis; nevertheless, this might cause the symptoms to reappear. Further, while hormone-based therapy that lower oestrogen levels do enhance clinical results<sup>[22]</sup> Night sweats and hot flushes are other typical side effects of this. An older premenopausal woman has a higher chance of experiencing menopause following adjuvant chemotherapy, and the chance of ovarian failure is affected by the kind and dosage of chemotherapy.<sup>[23]</sup> The risk of early menopause is increased when oophorectomy is combined with tamoxifen, compared to chemotherapy alone.<sup>[22]</sup> Tamoxifen causes hot flashes in as many as 80% of women who take it, and 30% of those women say the flushes are quite bad<sup>[24]</sup> and Hot flashes are three times more severe and occur more frequently in women who have undergone an oophorectomy as compared to those who experience menopause naturally.<sup>[25]</sup> Women using adjuvant hormone treatment in addition to chemotherapy had the greatest rise in hot flushes, according to a prospective longitudinal research.<sup>[26]</sup> Additionally, menopausal symptoms may persist for up to ten years if therapy is prolonged.<sup>[22]</sup> So, unlike women experiencing menopause due to natural causes, women with breast cancer may experience a more rapid and prolonged onset of menopausal symptoms.

### Traditional Medicine and Its Limitations

Breast cancer patients now have access to effective treatment options such as hormone therapy, radiation therapy paired with adjuvant chemotherapy, and surgical removal of the cancerous tumour.<sup>[27]</sup> Radiation therapy and breast-conserving surgery are the standard treatments for breast cancer in its early stages, stages I and II. After breast-conserving surgery, radiation treatment lowers mortality and recurrence rates.<sup>[28]</sup> Patients with early-stage breast cancer who have surgery and radiation therapy run the risk of developing brachial plexopathy, rib fracture, tissue necrosis, pericarditis, and second non-breast infeld malignancies, according to reports.<sup>[29]</sup> The sole systemic medication that has been shown effective in treating TNBC is "chemotherapy." Another major cause of cancer-related mortality is multidrug-resistant (MDR) tumours, which pose a hazard to cancer therapy. Drug resistance is a serious problem, therefore it's crucial to learn what causes multidrug-resistant bacteria and how to treat them.<sup>[30]</sup> Modification of drug efflux membrane transporters, specifically P-glycoprotein, MRP 1, and BCRP, is one of the intricate processes that contribute to the development of drug resistance.<sup>[32,32]</sup>, and alterations in beta-tubulin<sup>[32]</sup>; The MRP family has nine members, designated as MRP1–9.<sup>[33]</sup> Anthracyclines (doxorubicin, daunorubicin, epirubicin, and mitoxantrone), taxanes (paclitaxel, docetaxel), and capecitabine are among the many once effective medications that patients may develop resistance<sup>[34]</sup>, Fumoleau et al. recommend monotherapy for the treatment of breast cancer. In addition to being resistant to treatment, cancer stem cells can also retain their "stemness." Their capacity to replenish tumour masses with fresh cancer cells repeatedly sets them apart.<sup>[35]</sup> Anaemia, due to a decrease in the cells' ability to carry oxygen, and an infection, due to a decrease in white blood cells, are two serious side effects of chemotherapy. Hair loss as a result of traditional therapy is another major adverse effect. As a result of these therapies, you may also have the following side effects: fatigue, sore throat, nausea, ulcers, decreased appetite, altered taste perception, altered bowel habits (constipation or diarrhoea), altered skin tone, and hormonal shifts.<sup>[36]</sup> In light of the above, it is critical to quickly identify a replacement method of breast cancer treatment that does not include the use of chemotherapy or radiation and does not carry the same risk of adverse effects.

### Regulation of herbal goods and online resources

Herbal medicine specialists focus on addressing long-term health issues, however people sometimes self-medicate with herbal remedies for more minor ailments.<sup>[37]</sup> Herbal medicine may be more prone to negative side effects than other forms of complementary therapy

because of the wide variety of plants that may contain active components.<sup>[37]</sup> The lack of product certification and standardisation makes it difficult to know if botanicals are safe to use. Unrefined plant extracts including many components or herb mixes may also be present in the herbal product.<sup>[37]</sup> Herbal items offered in supermarkets and other retail outlets often do not include contra-indications, despite the numerous reported interactions of botanical medicine with prescription pharmaceuticals.<sup>[38]</sup> Herbal components are regulated differently in different countries. Commission E, a German expert group, was formed in 1978 by the German government to assess the efficacy and safety of more than 300 plants and herb combinations supplied in Germany. It wasn't until 1998 that the American Botanical Council brought the Commission E Monographs into the country. Despite this, a number of the monographs were rather short, none of them included citations for relevant research, and the harmful impacts were not thoroughly detailed.<sup>[39]</sup> Consumers are advised to purchase only herbs with drug identification numbers to guarantee they are purchasing a product that has been evaluated, as the status of herbs in Canada has been changed from food supplements to pharmaceuticals by the Natural Health Products Directorate (Health Canada).<sup>[40]</sup> A lot of herbs in Germany are sold with a prescription, and new laws in France limit the amount of approved herbal products that pharmacies may sell. Among Europe's primary herbal medicine regulating and registration organisations are the European Herbal Practitioners Association, the National Institute of Medical Herbalists, and the Register of Chinese herbal medicine.<sup>[37]</sup> The European Directive on Traditional Herbal Medicinal Products regulates herbal medicines in the European Union. All over-the-counter herbal medications in the UK will be required to verify with the Traditional Herbal medications Registration Scheme after April 2011, marking the complete implementation of this rule that was put in place in 2005.<sup>[41]</sup> Published in 2009 and due for periodic updates, the European Food Safety Authority's publication provides guidelines for the evaluation of botanicals' safety.<sup>[42]</sup> Herbal remedies in the United Kingdom are overseen by the Medicines and Healthcare products Regulatory Agency (MHRA). Anyone looking for evidence-based information about herbal products and other complementary and alternative medicine options can peruse a list of websites that have been hand-picked for this purpose.<sup>[41]</sup>

### **Present situation and potential future impact of breast cancer**

Worldwide, breast cancer is the most common malignancy in women and ranks high among the most common cancers detected to date. In 2018, 0.62 million people lost their lives to breast cancer, and 2.08 million new cases were detected, making it 11.6% of all cancers

reported, according to the International Agency for Research on Cancer (IARC) Globocan statistics.<sup>[44]</sup> If things continue as they are, by 2040 there will be 3.05 million incident cases and a terrifying 6.99 million fatalities.<sup>[45]</sup> At least once throughout their lifetimes, about 10% of women will get a breast cancer diagnosis.<sup>[43]</sup> Both developed and developing nations are witnessing a steady increase in the incidence of breast cancer, according to epidemiological observations.<sup>[46]</sup> Genetics is thought to account for about 10-15% of breast cancer cases, whereas environmental and lifestyle factors are the primary determinants of breast cancer risk.<sup>[47]</sup> characteristics that increase a woman's chance of developing breast cancer include her age (>50), her family history of the disease, and her reproductive history, including characteristics such as early menarche, nulliparity, late pregnancy, or menopause.<sup>[48]</sup> Another recognised risk factor for this condition in postmenopausal women is the long-term use of oral contraceptives or hormone replacement treatment.<sup>[49]</sup>

**Table 1: Ayurvedic treatment plan in phase -1 (Adjuvant with chemotherapy).**

S. No.	Medicine	Directions	Dietary recommendations	Principal outcomes
1.	Aswagandha	take one 3g pill twice day	Completely unrestricted. assistance in avoiding chemotherapy for cancer	preventing chemotherapy-induced neutropenia is one of the anticancer effects.
2.	Yastimadhu	3g daily with a glass of water after breakfast	Drinking pomegranate juice every day alongside carrots and tomatoes	Reduces chemotherapy-related adverse effects by increasing blood cell, platelet, and haemoglobin counts.
3.	Vincarosea flower	Start with an empty stomach and work your way up to taking the flowers. Soak the flowers in 100 cc of water overnight, then strain, remove, and drink the water.	Completely unrestricted.	In order to deal with the breast cancer that has been found. Great progress made in just eight months. A comprehensive PET CT scan revealed no signs of metastases or secondary malignancies. Cleared axillary and skeletal lesions
4.	Mahayogaraja guggulu	Three times daily, take one pill.	Take with or without food.	Structural lesions and chronic discomfort affecting the patient's right side

**Table 2: Ayurvedic treatment plan in phase -2 (definitive/ without any chemotherapy).**

S. No.	Medicine	Directions	Dietary recommendations	Principal outcomes
1.	Eladi gutika	twice daily, take two pills	Completely Unrestricted Diet	Causes of the patient's respiratory symptoms (pleural effusion)
2.	Talisadi churnam 2g 3 times with honey	Using honey three times, 2 g	Completely Unrestricted Diet	Causes of the patient's respiratory symptoms (pleural effusion)
3.	Vincarosea flower	Start with an empty stomach and work your way up to taking the flowers. Soak the flowers in 100 cc of water overnight, then strain, remove, and drink the water.	Completely Unrestricted Diet	In order to deal with the breast cancer that has been found. Great progress made in just eight months. A comprehensive PET-CT scan of the body revealed no signs of metastases or secondary malignancies. Tumours in the skeleton and the axilla have healed.
4.	Mahayogaraja guggulu	Twice day, take one pill.	Take with or without food.	Structural lesions and chronic discomfort affecting the patient's right side

### Cancer therapy with ethnomedicine and herbal substances

From the very beginning of our species, plants have met our most fundamental needs, including those for sustenance, fibre, housing, and healing. As a result, plants have played an essential part in our survival and evolution. Many of the world's oldest medical practices, including Ayurveda, Unani, and Chinese traditional medicine, have their roots in the use of plants to treat illness. Herbal medicine is the go-to for many people in developing and impoverished nations when it comes to basic health care. Popularity of traditional herbal remedies is driven by their abundance, low or nonexistent adverse effects, and affordability. Finding pharmacologically similar compounds in plants that have long been utilised for medical purposes has recently become a focal point of plant study across the world. Curcumin, resveratrol, quercetin, and a plethora of other naturally occurring plant-based chemicals have demonstrated encouraging anticancer properties and are now being considered as potential adjuvant chemotherapy agents. On top of that, chemicals found in nature are less harmful to normal cells and can even selectively kill out sick ones.<sup>[50]</sup> This could explain why many pharmaceuticals on the market today have molecular structures that are quite close to those of substances found in nature. It is possible that herbal substances might help prevent cancer in its early stages by exhibiting a variety of anticancer activities, including antioxidant, anti-inflammatory, antimutagenic, and apoptosis-inducing properties.



Breast cancer prevention and treatment may be aided by dietary consumption of these herbal products in sufficient amounts. They accomplish this by halting cell cycle progression, inducing apoptosis, controlling carcinogen metabolism and oncogenic expression, inhibiting cell adhesion, proliferation, and migration, and blocking signalling pathways vital to cancer progression.<sup>[51]</sup> Worldwide, 136 anticancer medications were introduced between 1981 and 2014, with about 83% of those being herbal substances or their derivatives.<sup>[52]</sup> Vincristine, vinblastine, paclitaxel, and docetaxel are among the anticancer medications that are now used to treat breast cancer. Few herbal medications are advancing into the preclinical or clinical stages, despite their effectiveness in treating breast cancer and its complications.

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