International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 4 July-Aug 2024, pp: 1062-1070 www.ijprajournal.com ISSN: 2456-4494

An Organised Analysis of Herbal Remedies for Breast Cancer Treatment

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Date of Submission: 01-08-2024 Date of Acceptance: 10-08-2024

ABSTRACT
Breast cancer continues to be one of the most common malignancies among women globally, prompting extensive research into innovative treatment approaches. This review article looks at the effectiveness, mechanisms of action, and prospective integration of herbal medications into traditional treatment plans in the therapy of breast cancer. The paper also looks at the safety profiles, pharmacokinetics, and possible interactions between various herbal remedies and conventional hormone therapy and chemotherapy. This review attempts to give a thorough overview of the therapeutic potential and difficulties of integrating herbal medications into breast cancer treatment protocols by combining the available data, providing ideas for further study and clinical use.
Keywords: Breast cancer, herbal drugs,anti-cancer activity,Echinacea.

I. INTRODUCTION:

A major global health concern, cancer is a hereditary disease caused by mutations in the genetic code that control how cells behave [1]. Globally, breast cancer is the primary cause of cancer-related death for women, accounting for over 500,000 fatalities. Oestrogen receptor alpha (ERα) is closely linked to the pathophysiology of breast cancer and plays a significant part in the normal physiological activities of mammals [2].

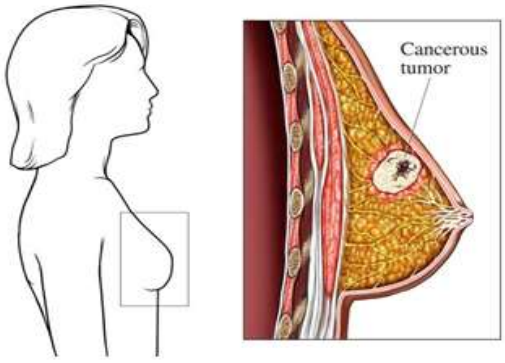

Fig. 1: Breast Cancer.

Although there are numerous varieties of breast cancer, invasive carcinoma and ductal carcinoma in situ (DCIS) are the most prevalent types.Others are less prevalent, like phyllodes tumours and angiosarcoma[3]. According to the National Cancer Institute (NCI), cancer avoidance is a useful strategy for lowering the number of people who get the disease [4]. Age, food, elevated hormone levels, and alterations in the environment are the primary risk factors for breast cancer. Early identification of breast cancer boosts the patient's chance of survival, thanks to significant advancements in medical science. However, the course of treatment results in several adverse consequences and lowers the cancer patient's quality of life [5].Chemotherapy, hormone therapy, radiation therapy, and surgery are common therapies for breast cancer. But these come with more harmful side effects that could harm the patient more severely [6].Since the particle diameters of nanoscale systems are 1 μm, they are also referred to as sub-micrometer systems. These days, the therapeutic process has significantly improved because to the efficient usage of nanoparticles in conjunction with herbal ingredients. Several examples include Quercetin, Topotecan, Shikonin, Berberine, Artemisinin, Cinnamaldehyde, Vincristine, and Thymoquinone[7].

Pathophysiology of breast cancer:

Breast cancer is a complex disease that, depending on factors such as distance, stage, and histological similarity, can have varying prognoses and treatment responses. Breast carcinoma is expected to arise by a multi-step process that involves the anti-methylation promoter activating oncogenes and a malignant tumour.

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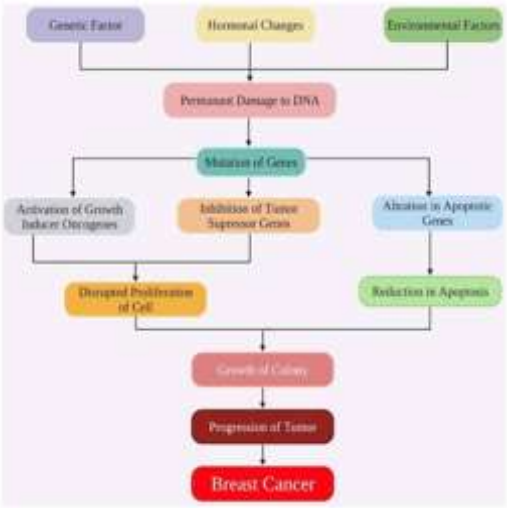

Fig. 2: Pathophysiology of breast cancer

This mechanism is similar to other forms of human cancer. One of the fundamentalprocesses in the development of malignant tumours, such as breast cancer, is hypermethylation. In carcinogenesis, this promoter methylation is not dispersed randomly; rather, it is genetically associated with a particular kind of cancer. Distinct methylation patterns of various genes have been found in distinct histological subtypes of breast cancer. Using paraffin-filled fixed tissue blocks, invasive breast cancer will be molecularly subtyped according to its colour response to rabbit monoclonal antibodies against the oestrogen receptor (ER), progesterone receptor (PR), and her-2 neu[8].

Sr. no.	Name of plant	Part used	Activity	Reference
1.	Curcumalonga(Turmeric)	Rhizome	• Inhibitionof ornithine activity. • Decarboxylase Activity. • Anti Proliferative. • Antitumorigenic.	[9]
2.	Urticadioica (Stinging nettle)	Leaves	Anti-proliferative	[10]
3.	Echinacea(Estern purple coneflower)	Flower.	Cytotoxicity.	[11]
4.	Withaniasomnifera(Winter cherry)	Roots/Leaf	Chemopreventive Efficacy	[12]
5.	Rheum emodi(Rhubarb)	Rhizome	Cell migration inhibition efficiency	[13]

Table: Herbal drugs used in treatment of breast cancer.

1] Curcuma longa linn:

Biological properties of curcumin :

Curcumin has a broad range of biological effects that include prevention of cancer, ischaemia, inflammation, and ageing. Additionally, curcumin has strong antioxidant qualities. By reducing the quantity of oxidative, damaging, and cancer-causing DNA molecules in tissue samples, it can stop or reverse DNA damage[14].

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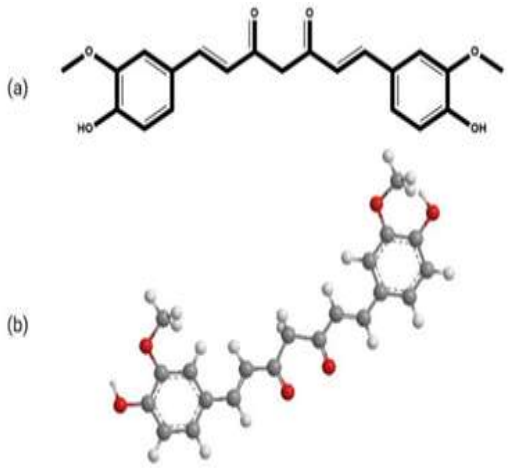

Fig.3:(a) structure of Curcuma, (b) 3D structure of curcuma

Anti-cancer activity of curcumin :

Over the past few decades, there has been a concerning rise in the number of women dying from breast cancer[15].Multitargeting of various pathogenic signalling pathways is thought to be a key trend in the fight against drug-resistant BC cells in order to get the best possible therapeutic results. To more effectively treat BC, researchers are looking for promising medication candidates[16].Breast cancer recurrence rates remain high even after chemotherapy, radiation therapy, lumpectomy, and endocrine therapy, according a meta-analysis of 21 retrospective studies[17]. Therefore, more potent therapeutic approaches are still required. Curcumin therapy significantly decreased telomerase activity in a study using MCF-7 breast cancer cells and MCF-10A normal mammary epithelial cells[18].The EZH2 oncogene is first downregulated by CUR through activating the extracellular regulatory protein kinase (ERK), p38 kinase, c-Jun amino-terminal kinase (JNK), and extracellular regulatory protein kinase (MAPK). This pathway also inhibits the expression of HIF-1α and HIF-2α, suppresses the expression of EGFR and HER-2/neu, increases p53 phosphorylation, decreases VEGF and basic fibroblast growth factor (b-FGF) transcript levels, suppresses the expression of ER downstream genes pS2 and TGF-β, and suppresses the activity of EGFR and HER-2/neu to inhibit BC cell proliferation[19]. Moreover, it has been shown that CUR inhibits cell division in BC cells by triggering cycle arrest and the development of unipolar spindles in the late G2M and S phases[20].

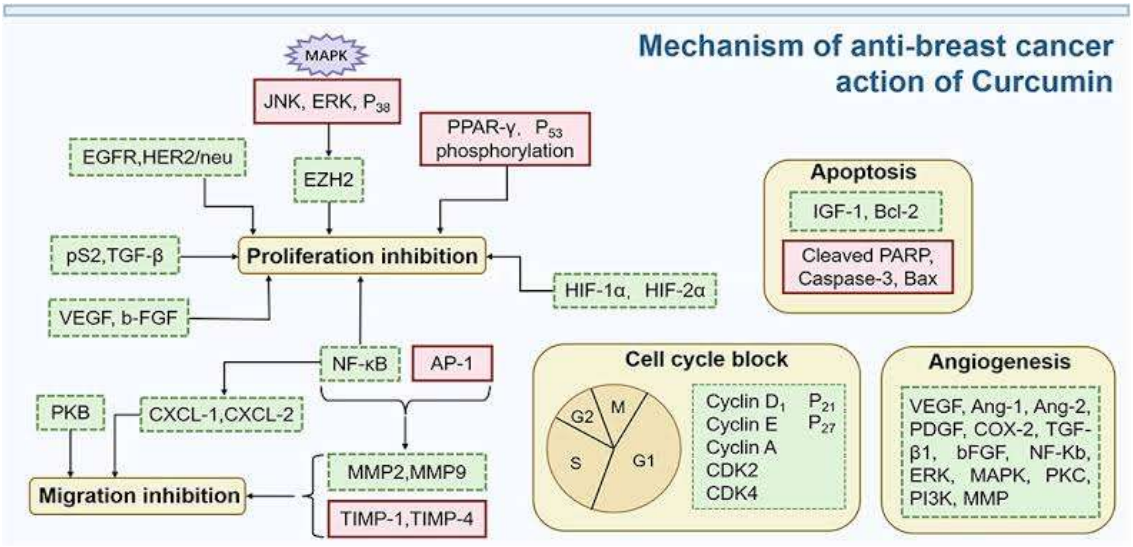

Fig. 4: Mechanism of anti-cancer action of curcurcumin

Finally, CUR causes BC cells to undergo apoptosis by upregulating insulin-like growth factor 1 (IGF-1), cleaved PARP and caspase-3 expression, pro-apoptotic protein (Bax) expression, and anti-apoptotic protein (Bcl-2) expression[21]. In addition, CUR suppresses the expression of transforming growth factor-β1 (TGF-β1), angiopoietin-1 (Ang-1), angiopoietin-2 (Ang-2), platelet-derived growth factor (PDGF), cyclooxygenase-2 (COX-2), and basic fibroblast growth factor (bFGF). It also inhibits the production of NF-κB, extracellular-signal regulated

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kinases (ERK), MAPK, protein kinase C (PKC), phosphoinositide 3-kinase (PI3K), and matrix metalloproteinases, which are all involved in tumour angiogenesis. It has the potential to limit the carcinogenic effects of immunosuppressive cytokines, including IL-10 and transforming growth factor beta (TGF-β), as well as lessen the loss of T cells throughout the carcinogenesis process[22].

2]. Urticadioica

A perennial herbaceous grass with branching legs, nettle is scientifically known as Urticadioica. Straight and square shoot with coated bitter Azkrk leaves. It is visible in the hive Shemiranat, the wile in Iran next to Tehran, Karaj on the Alborz hills, and the northern districts of Mazandaran, Gilan, and Drazrbayjan, on the slopes of Sahand, Zanghab, and Lorestan (in the river)[23].The therapeutic qualities of Urticadioica, sometimes referred to as stinging nettle, are linked to a number of health benefits. Its astringent, depurative, galactogogue, diuretic, nourishing, and stimulating qualities are a few of these, along with its capacity to lessen inflammation and asthmatic symptoms[24].There are several phenolic compounds in it, which are well-known aromatic compounds with comparatively small molecular weights. Benzene rings are joined to one or more hydroxyl groups to form these compounds, which are commonly seen in association with sugars, also referred to as glycosides. The quantity and location of hydroxyl groups in glycosides that are formed by phenols affect their action. The quantity of carbon atoms in each of these compounds' chemical structures determines which grouping they belong too[25].Because urticadioica leaves are so high in essential fatty acids, they are an important and beneficial source. Due to their vital function in controlling human metabolism, the search for sources of fatty acids has become increasingly important in recent years. These fatty acids are recognised to have a beneficial effect on cancer prevention and to have good antioxidant capabilities. For this reason, the significant amount of fatty acids found in Urticadioica leaf tissues is extremely important for enhancing human health[26].

Anticancer Activities of Urticadioica:

We discuss the biology of U. Dioica in detail, including how it may stimulate or block key metabolic processes in cells and trigger apoptotic pathways, both of which have been connected to anti-tumor effects. Recent studies have demonstrated U. Dioica's cytotoxic and anti-cancer properties, particularly against cancers of the breast, stomach, lung, colon, and prostate.The principal anti-tumor activities of U. Dioica against several human cancer cell lines and animal models will be discussed in this section. One class of disorders called cancers is caused by unchecked proliferation of normal cells that infiltrate and spread to other parts of the body.Unfortunately, it continues to be the world's largest cause of death, with intolerably high rates of both incidence and mortality[27].

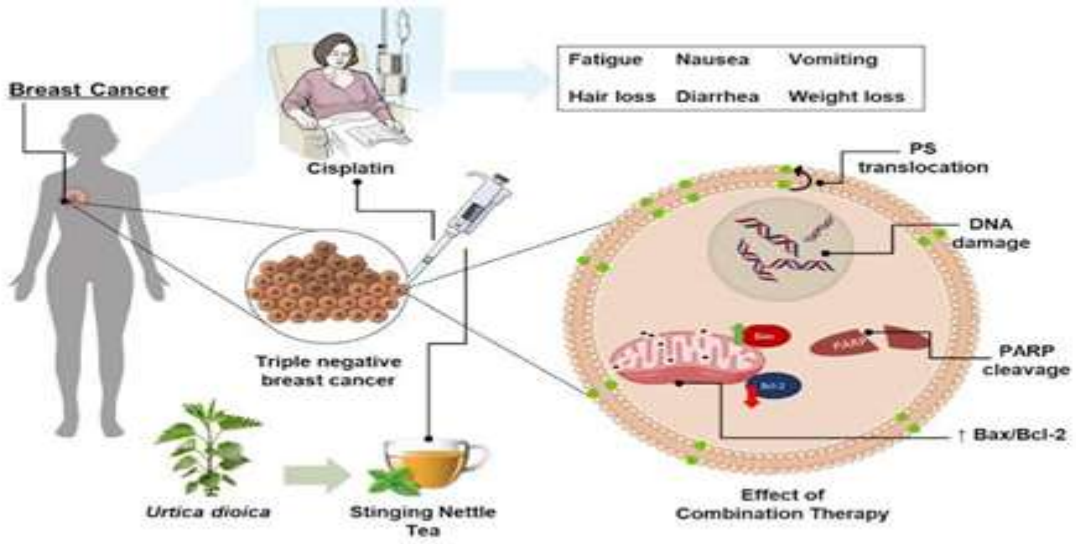

Fig. 5: Anti-cancer activity of Urticadioica

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The activity of the U. Dioica leaf aqueous extract was investigated using the human breast cancer cell line MCF-7. The extract from U. Dioica shown antioxidant and anti-proliferative properties. After being exposed to different concentrations of the U. Dioica extract for 24, 48, and 72 hours, significant cell killing was observed in a dose-dependent manner, with an IC50 value of 2 mg/mL concentration after 72 hours of treatment.according to earlier studies on anticancer medications[28]. In particular, U. Dioica leaves have the potential to prevent cancer by lowering the elevated degree of oxidative stress seen in cancerous cells. This is because there are significant amounts of compounds in the leaves that have the ability to scavenge free radicals and act as antioxidants[29].

3]. Echinacea :

A member of the Asteraceae family, echinacea is used in traditional herbal and medical practices. Despite being cultivated in Europe, this herbaceous perennial aromatic plant is native to North America[30]. Out of the nine species of Echinacea, three are commonly used in phyto-therapeutic preparations. These three are Echinacea pallida, Echinacea purpurea, and Echinacea angustifolia. Eighty percent of the commercial products made from Echinacea contain medical uses for the roots, rhizomes, and flowering sections of the three species[31]. With its abundance of flavonoids, echinacea is a popular herbal supplement that is widely used for its anti-inflammatory, antioxidant, and immune-stimulating qualities [32].

Anticancer Activitie of Echinacea:

Echinacea-containing herbal supplements are commonly taken by cancer patients[33]. The use of echinacea by patients with breast cancer has not been well studied [34].The potential of echinacea for anti-tumor therapy was investigated through in vitro study. It was found that extracts from Echinacea purpurea were more effective than those from Echinacea Pallida in inhibiting the proliferation of the BT-549 murine breast cancer cell line[35]. The Echinacea Pallida root's pentadeca-(8Z, 13Z)-dien-11-yn-Z-one component inhibited the proliferation of the MCF-7 breast cancer cell line [36].Echinacea angustifolia root components (ethyl acetate fraction and chicoric acid) and doxorubicin boosted cell proliferation of MCF-7 breast cancer cells, potentially interfering with the anti-cancer drug's efficacy [37].An in vitro study found that treating MCF-7 breast cancer cells with hexane fractions of Echinacea purpurea reduced growth, and cynarin from Echinacea angustifolia roots similarly demonstrated anti-proliferative activity[38].

4]. Withaniasomnifera:

Withaniasomnifera, also known as Ashwagandha, Indian Ginseng, or winter cherry, is a well-known herb that has been used for centuries in Ayurvedic medicine to increase lifespan, vitality, and as a health-promoting tonic (rasayana) to strengthen the body's resistance to diseases[39].Withaniasomnifera is an erect, greyish, slightly hairy evergreen shrub with relatively long tuberous roots and a short stem. The stem and branches are coated with minute star-shaped hairs, and the leaves are simple, up to 10 cm long, oval, petiolate, and alternating. Flowers are small and greenish or yellow, appearing alone or in small clusters in the leaf axils and blooming almost all year. The fruit is smooth, globose, and meaty, with many seeds that become orange-red when ripe. It has a membrane covering. This tiny, woody shrub grows to approximately 2 feet tall and is widespread in Africa, India, the Mediterranean area, and the United States[40].In India, W. Somnifera is commonly cultivated for medicinal purposes using several chemotypes[41]. Of the 26 species in the genus Withania, only two—W. Somnifera and W. Coagulans Duna—are found in India. A third species, W. Obtusifolia (Tackh), was discovered in South India[42].

Antitumor activity of W. Somnifera:

Rats previously treated with the breast carcinogen methylnitrosourea (MNU), which functions as a mammary cancer inducer, were given W. Somnifera roots. W. Somnifera root extract-treated rats had up to 23% fewer tumours overall than control rats, according to experimental results. The root extract dose was administered at 150 mg/kg of body weight during the trial, and the control rats did not receive an MNU injection[40]. The cytotoxicity of this plant's ethanolic root extract was assessed[43].It also opposes the cell line that causes breast cancer. Cell apoptosis, DNA fragmentation, and cell cycle analysis were among the aspects of cell growth and degeneration that they observed, and they used the anticancer drug doxorubicin as a standard for comparison study. They also found that the ethanolic extract had a dose-dependent cytotoxic effect on breast cancer cell lines. Evaluation of the cytotoxicity of W. Somnifera extract in ethanol and the commercial anticancer drug doxorubicin is a significant component of this study. Results indicated that

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while W. Somnifera extract was non-cytotoxic to non-cancerous cells when compared to breast cancer cell lines, doxorubicin was cytotoxic to both cancerous and non-cancerous cells. Breast cancer patients' quality of life and the fatigue brought on by chemotherapy[44].

5]. Rheum emodi

Rheum emodi Wall. Ex Meissn., a leafy perennial herb in the Polygonaceae family, stands 3.0 m tall[45]. The leaves are huge (40 cm long), roughly oval, and radical, with a long, robust, and scabby petiole (30–45 cm). The stem is quite stiff and green, with brown streaks. The inflorescence is a panicle that is 0.6 to 0.9 m long, pubescent, upright branching, and green, with erect stern branches. Flowers measure 3 mm in diameter and range in colour from mild to reddish. Fruits are 1-2 cm long, ovoid to oblong, winged, and purple, with a cordiform base and an erose tip. The seeds are likewise winged [46]. Rheum emodi, often known as rhubarb, Indian rhubarb, or Himalayan rhubarb, is an essential medicinal herb utilised in the Ayurvedic and Unani systems of medicine [47].

Anti-cancer activity of rheum emodi:

We tested the effects of RE on human breast cancer cells MCF-7 utilising the MTT assay and cell morphological assessment. Photomicrographs clearly show the morphological changes that occur in the cells, i.e., the cells' shape altered dramatically from normal to rounded off, deformed, and at greater concentrations of RE. Morphological studies indicate that increasing the dose of RE causes a change in cellular morphology, resulting in cell death in MCF-7 cells.Cell mortality was statistically significant at greater concentrations of RE compared to lower doses of RE, as demonstrated by the cell viability data, which revealed that at the doses of 50 µg/ml, 100 µg/ml, and 200 µg/ml of RE, the percentage cell viability was 74.24%, 58.14%, and 38.18%, respectively.Based on their greater effectiveness, we have chosen three doses—50 µg/ml, 100 µg/ml, and 200 µg/ml—for additional research[48].

II. CONCLUSION:

The use of herbal drugs in the treatment of breast cancer shows considerable promise, offering potential benefits in terms of efficacy and reduced side effects compared to conventional therapies. Compounds such as Curcuma longa Linn(Turmeric), Urticadioica(Stinging nettle), Echinacea(Estern purple coneflower), Withaniasomnifera (Winter cherry), Rheum emodi (Rhubarb) have demonstrated various anticancer properties, including the ability to inhibit tumor growth, promote apoptosis, and enhance the efficacy of standard cancer treatments.However, while preclinical studies and some clinical trials have provided encouraging results, there remain significant challenges to the widespread adoption of herbal therapies in clinical practice. Key obstacles include the need for standardized formulations, comprehensive understanding of pharmacokinetics, and thorough evaluation of potential interactions with conventional therapies.Ultimately, while promising, the use of herbal drugs in breast cancer treatment should be approached with caution until further evidence is available. With ongoing research and clinical validation, these natural compounds could become valuable components of personalized cancer care, improving outcomes and quality of life for patients.

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