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Review article

Understanding the prophylactic, chemo preventive, and pharmacotherapeutic perspectives of various dietary foods in breast cancer

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ABSTRACT

Currently, one of the most challenging diseases to tis breast cancer. Hormone therapy, surgery, chemotherapy, and radiation have all been used to treat breast cancer for a long time, but they are become eating less and less successful due to serious side effects and rising drug resistance. Numerous dietary foods have been linked to altered cancer genesis and progression pathways, decreased aggressiveness, and growth inhibition of malignant cells. These dietary foods may be advantageous compared to produce medications since they exhibit lower toxicity and negative effects in various investigations. The promises made by dietary foods for breast cancer treatment by focusing on several pathophysiological cascades involved in the onset and progression of breast cancer and their capacity to simultaneously stop metastatic and growth progression. Some of the extensively researched numerous dietary foods that specifically target certain breast cancer pathways and express any of the three attributes are mentioned in article.

Keywords: Breast, Cancer, Dietary Foods, Chemoprevention, Therapy, Prophylaxis.

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INTRODUCTION

By 2030, cancer will be the greatest cause of death and sickness worldwide, taking the lives of almost 21 million people. Unrestrained cell division causes genetic instability and change. Breast cancer (BC), which affects an estimated 1.5 million women each year [1], causes more than 5 lakh women to pass away each year. In the majority of countries, BC is the most common kind of cancer seen in women, making up 25% of all female cancer diagnoses. It is the main factor in female cancer-related mortality. Economically developing countries account for more than half of new BC diagnoses and more than half of the disease's mortality. BC is the leading cause of cancer mortality in women, followed by cervical, colorectal, and lung cancer [2]. 4 lakh new instances of invasive BC will be found in women in 2025, while >5000 new cases will be found in males. >50 thousand women and >1 thousand men will perish this year as a result of BC. The overall lifetime risk for a woman includes deaths from other causes that could take place before she is given a BC diagnosis. Up to 75% of BC patients in middle- and low-income countries have stage-III or stage-IV illness, according to research [3]. Around 65% of all cancer deaths worldwide occur to patients in middle- and low-income nations. This is partially because there are few available treatments and many people arrive with a disease that has evolved to the point where it is now incurable. Patients in middle- and low-income nations usually have limited access to chemotherapy, radiation, and surgery, which causes unnecessary suffering and early mortality [4].

An estimated 2.5 million new cases of BC are reported each year, making it the primary cause of cancer-related mortality among females. In 2018, 7 lakh women lost their lives to BC. By 2030, there will have been around 12.5 million additional instances of BC reported, making it the most common illness worldwide. After receiving treatment for BC, a woman and her family may have a variety of detrimental repercussions on their physical and mental well-being, as well as their quality of life and financial security [5]. Due to their severe side effects and the emergence of drug resistance, therapeutic procedures are becoming more ineffective. The utilization of alternative medicine techniques in this instance, however, may be a wise decision given that DFs have been demonstrated to have strong anticancer potential. Natural substances that can inhibit the development of cancerous cells and control processes connected to cancer may be used to treat BC. Dietary foods have been important in

the treatment and prevention of cancer. Foods, nutraceuticals, herbal drugs, and other natural resources have been identified to have anticancer properties [6]. The negative effects of dietary items made from plants are far less severe than those associated with traditional chemotherapy. Effective medicines must be created in order to prevent, lessen, or reverse the development of BC in high-risk women. Since dietary items have less adverse effects and a lower toxicity than produced medications, they may be a viable chemoprevention strategy for BC [7].

This review article is highly beneficial for the readers regarding the effectual roles of day-to-day foods (vegetables, fruits, and spices) wherein an understanding pertaining to the plausible benefit of dietary foods as compared to therapeutic treatment are comprehensively highlighted in context to the prophylactic, chemo preventive, and pharmacotherapeutic perspectives against breast cancer.

Carcinogenesis mechanisms in breast cancer

The arachidonic acid route, a metabolic process, is crucial to carcinogenesis. Phospholipase A_2, cyclooxygenases, and lipoxygenases, as well as their metabolic byproducts prostaglandins and leukotrienes, have been considered prospective targets for the prevention and therapy of cancer in this respect. Tumor cells frequently experience hypoxia because the oxygen supply to tumor tissues has diminished. In tumor cells, hypoxia-inducible factor-1 (HIF-1) signaling is stimulated, which enables them to endure under these hypoxic conditions. When HIF-1 is active, several HIF-1 target genes are expressed, including those involved in cellular proliferation, invasion, metastasis, cancer stemness, and metabolic reprogramming. These mechanisms are brought on by HIF-1 activation. HIF-1 is thus considered to be a potential drug target for the treatment of cancer [8].

The enzyme aromatase transforms androstenedione and testosterone into estrone and estradiol. Breast adipose stromal fibroblasts, which primarily synthesize aromatase mRNA from promoter, may exhibit physiological levels of aromatase. When a certain subset of aromatase promoters is activated by BC, there is an increase in the expression of the aromatase gene that supports BC. Apoptosis is a crucial mechanism of controlled death and is known to take place in the absence of cell damage or external stress [9]. Apoptosis is tightly regulated by many kinds of executioner and regulator molecules. Cells die by apoptosis when their capacity to attach to extracellular matrixes is compromised by chromatin condensation, nuclear DNA damage, and cell shrinkage. Caspases are triggered and phosphatidylserine is externalized, which causes cell death. Patients with BC frequently exhibit resistance to the EGFR-TKIs gefitinib and other EGFR-TKIs. Molecular parameters for predicting sensitivity to EGFR-TKIs are essential for properly conducting and organizing future research [10].

Carcinogenesis is typified by anomalies in genetic appearance as well as genetic and epigenetic changes. Epigenetics refers to a change in gene expression programming without a matching alteration in DNA sequence. Along with DNA methylation and covalent changes of histone tails, non-coding RNAs are essential for healthy development and genomic stability. Bioactive substances included in food and herbs have been demonstrated to influence gene expression by focusing on different elements of the epigenetic machinery [11]. The estrogen receptor acts as a prognostic marker and an efficient target for a number of estrogen ligands in the treatment of BC that is hormone-dependent. The ER subtypes ER and ER, which are mostly G-protein-coupled receptors, are activated by estrogen, notably by 17-estradiol. Activation is followed by translocation into the nucleus and contact with DNA, which regulates the activity of many genes. Through genomic activities, ERs are able to regulate RNA synthesis without directly binding to DNA [12].

Dietary foods for prophylactic use against breast cancer

Apple

Apples are a common food in human diets and are consumed often. Flavonoids extracted from apple peel and flesh suppressed the growth of MCF-7 BC cells [13]. Further investigation revealed that the high polyphenol content of Pelingo apple juice has an antiproliferative effect on MDA-MB-231 and MCF-7 cells. The addition of Pelingo juice also inhibited the development of colonies and TPA-induced ERK1/2 activation of pre-neoplastic cells [14]. On MDA-MB-231 and MCF-7 cells, apple extract had a significant antiproliferative effect. Apple extract also significantly slowed down the cell cycle in MCF-7 cells by lowering the levels of the protein's cyclin D1 and Cdk4. Apple extract and 2-hydroxyursolic acid, which is isolated from apple peel, may inhibit the NF-κβ activation caused by TNF-α in MCF-7 cells [15]. 2-hydroxyursolic, which likewise displayed antiproliferative and pro-apoptotic effects on MDA-MB-231 cells, controlled the p38/MAPK signal transduction pathway. Apple-derived peptides may also increase apoptosis, restrict cell growth in BC cells *in vitro*, and stop tumor metastasis in BALB/c mice by overexpressing p53. The synergistic effects of quercetin-3-D-glucoside and apple extract on MCF-7 cell proliferation were observed [16].

Black Cumin

Black cumin was recognized medication for more than 2 millenniums. The ability of black cumin to prevent cancer has recently drawn a lot of interest. An antimetastatic and proapoptotic effect of the supercritical CO_2 extract of black cumin on MCF-7 cells

was demonstrated *in vitro* [17]. Black cumin's proapoptotic and anti-proliferative effects of extract were discovered to be mediated through the p53 and caspase pathways. The seeds contain thymoquinone, which has potent anticancer and anti-inflammatory effects. But there was a preliminary hint that TQ may be an Akt inhibitor. Apoptosis-inducing Bcl-2 family members BAD and GSK-3 might be combated by activating Akt, which would then increase cell survival. All three MCF-7, MDA-MB-468, and T-47D cell lines were prevented from going into apoptosis by the TQ-induced suppression of Akt phosphorylation. TQ prevented tumor growth in mice bearing BC xenografts, perhaps as a result of ROS-induced p38 phosphorylation. TQ may also alter the PPAR-activation pathway and the PI3K/p38 kinase pathway, both of which control COX-2 expression and prostaglandin E_2 production, and this might explain TQ's antiproliferative effects on BC [18].

Capsicum

It has been proven that the red chili pepper ingredient capsaicin inhibits the proliferation of BC cells. After 24 hrs of capsaicin injection, MCF-7 cells were made to undergo apoptosis *in vitro* by a caspase-independent method. Capsaicin caused MCF-7 cells to undergo apoptosis, which was associated with mitochondrial dysfunction [19]. Additionally, *in vitro* BC migration and development were inhibited by capsaicin. Without causing any obvious side effects, capsaicin decreased the number of BCs in mice by 50% and delayed the progression of preneoplastic breast lesions by 80% *in vivo*. These effects were mediated by the EGFR/HER-2 pathway. Despite this, the question of whether capsaicin contributes to the growth of cancer is still up for dispute. It has been demonstrated that capsaicin is mutagenic and may increase the risk of cancer in people [20].

Citrus Fruits

Citrus fruits include oranges, lemons, grapefruits, pomelo, and limes. The anti-BC qualities of citrus fruits have recently attracted a lot of attention. Citrus fruit eaters in the study had a lower risk of developing BC than non-consumers. The citrus peel's polysaccharides decreased angiogenesis by reducing tube formation when used with human umbilical vein vascular endothelial cells and MDA-MB-231 cells [21]. Citrus fruit extracts from phalsak promote apoptosis in BC stem cells with anoikic resistance. Additionally, it led to cell death in MCF-7 cells by lowering bcl-2 gene activity and raising the expression of the bax and caspase-3 genes. Naringin has also been demonstrated to enhance apoptosis, block the G_1 cycle, and reduce the proliferation of malignant TNBC cells *in vitro* via modulating the activity of the catenin pathway. The citrus fruit flavonoid hesperidin, which has been found to be harmful, decreased the proliferation of MCF-7-GFP-Tubulin cells [22].

Clove

Clove is used both as a spice and a medicine by Chinese herbalists and chefs. Eugenol, the active component of clove, is primarily responsible for its bioactivities. *In vitro*, eugenol treatment slowed the proliferation and growth of MCF-7 cells and induced apoptosis. Following eugol treatment, lipid peroxidation increased while intracellular glutathione levels decreased. In human BCs, eugenol was found to exhibit proapoptotic and antiproliferative effects, which were ascribed to its targeting of the E2F1/survivin pathway [23,24].

Cruciferous Vegetables

Brussel sprouts, broccoli, cauliflower, watercress, and other cruciferous vegetables are cultivated and eaten all over the world. Cruciferous vegetables utilization was negatively correlated with BC risk. Cruciferous vegetables have demonstrated an anti-BC impact in experimental settings, which may be explained by their high glucosinolate content [25]. The myrosinase enzyme is produced when vegetables are sliced or chewed, which causes glucosinolates to break down into isothiocyanates. It has long been recognized that isothiocyanates, which comprise a range of substances including benzyl isothiocyanate, phenethyl isothiocyanate, and sulforaphane, have chemopreventive properties for many neoplasms, including BC. Additionally, indole-3-carbinol and its metabolites have anti-BC activity [26].

Garlic

For a very long time, garlic has been used as a spice all throughout the world. With an adjusted odds ratio of roughly 0.41, eating a lot of several Allium vegetables, especially garlic, may lower your risk of BC by nearly 40% [27]. The organosulfur components of garlic have been related to its anti-BC effects. Diallyl disulfide, the main organosulfur component in garlic oil, may cause MCF-7 cells to undergo apoptosis. Histone deacetylation inhibition, ERK activation, SAPK/JNK activation, and p38 activation may all promote apoptosis. In addition, the medication DADS inhibited the growth and spread of human BC [28]. The DADS therapy resulted in inhibition of the SRC/Ras/ERK pathway and elevated expression of miR-34a. MDA-MB-231 cell metastasis and growth were reduced as a result of this. The inhibition of the β-catenin signaling pathway by the DADS therapy also inhibited the metastasis and growth capacity of TNBC cells. It has also been demonstrated that diallyl trisulfide, which induces apoptosis, inhibits BC. Both MCF-7 cells and tumor xenografts experienced apoptosis as a result of excessive ROS generation and the subsequent activation of JNK and AP-1 [29]. By upregulating the expression of FAS, cyclin B1, cyclin D1, cyclin E, Bax, and p53 while downregulating the expression of Akt and Bcl-2 in response to the DATS treatment, apoptosis was also encouraged in

MCF-7 cells. DATS also reduced MMP2/9 activity by inhibiting the NF-κβ and ERK/MAPK signaling pathways, which in turn reduced TNBC cell motility and invasion. Additionally, DATS decreased estrogen receptor alpha expression and activity in T47D and MCF-7 cells. In the presence of Pin1, DATS treatment in MCF-7 cells caused a decrease in ER protein levels [30]. DATS may have yet another fresh target in BC stem cells: Q1 Forkhead Box. Pharmacological dosages of DATS inhibited SUM159 and MCF-7 cells in a dose-dependent manner, and this inhibition was associated with a decrease in FoxQ1 protein levels. S-allyl mercaptocysteine, an ingredient in garlic, caused apoptosis and placed MDA-MB-231 and MCF-7 cells in the G_0/G_1 phase of the cell cycle, respectively, suppressing their growth. Bax, Bcl-2, and Bcl-X-L were increased in the presence of SAMC treatment, and caspase-9 and caspase-3 were activated, indicating activation of the mitochondrial apoptotic pathway. Allicin, a major ingredient in garlic, inhibited TNF-α induced invasion and metastasis in MDA-MB-231 and MCF-7 cells but not MDA-MB-231 cells. By weakening the link between ER and p65 and decreasing the ERK1/2 and NF-κβ signaling pathways, VCAM-1 was inhibited [31].

Ginger

Worldwide, ginger has been used for culinary and medicinal reasons since the dawn of time. Recent research has suggested that ginger has anti-BC properties. Ginger methanolic extract was found to have an inhibitory effect on MDA-MB-231 cells during colony formation and proliferation that was dose- and time-dependent. Ginger extract also killed MDA-MB-231 and MCF-7 cells, increasing Bax and decreasing the levels of Bcl-2, NF-κβ, Bcl-X, Mcl-1, survivin, cyclin D1, and CDK-4. Two of the most well-known molecular targets of cancer, c-Myc and hTERT, had their expression reduced by ginger extract. Two bioactive components of ginger, gingerols and shogaols, may be in charge of its anti-BC actions [32]. Gingerols prevented the spread and proliferation of BC cells. By inhibiting cyclin-dependent kinases and cyclins in MDA-MB-231, 10-gingerol triggered a G_1 phase arrest. The 10-gingerol-induced suppression of Akt and p38 activity hindered the invasion of cancer cells. 6-gingerol hindered the migration and motility of MDA-MB-231 cells, which also resulted in decreased MMP-2/9 expression and activity [33]. By lowering MMP-9 expression by preventing NF-κβ activation, 6-Shogaol prevented MDA-MB-231 cell invasion. Six-shogaol also reduced the development of invadopodiums in MDA-MB-231 cells by lowering levels of the proteins c-Src kinase, cortactin, and MT1-MMP, which are invadopodium maturation regulators. 6-Shogaol may prevent BC cells from attaching to form a spheroid and hinder its growth and durability. This effect was brought about via secretase-mediated downregulation of Notch signaling and promotion of autophagic cell death [34]. 6-Dehydrogingerdione induced apoptosis and cell cycle suppression in G_2/M phase in MDA-MB-231 and MCF-7 cells through activating the ROS/JNK pathways. Clinical researches have also demonstrated the beneficial effects of ginger on BC patients. In comparison to those in the control group, people receiving an oral ginger supplement experienced significantly less nausea and vomiting episodes [35]. Patients with BC who breathed ginger essential oil reported significantly lower acute nausea scores, but there was no discernible difference in the overall therapeutic effect compared to those who did not. The patient's general health and appetite were improved by ginger aromatherapy, but vomiting was not reduced [36].

Grape

There is no doubting that grapes and their products, such as wine, are nutritious meals that are loved by people all over the world. In Balb/c mice implanted with 4T1 cells, it was demonstrated that dietary grape skin extracts significantly inhibited the lung metastasis of BC [37]. Grape skin polyphenols reduced cell migration in 4T1 cells *in vitro*, which may be related to the suppression of the PI3k/Akt and MAPK pathways. In a different study, grape seed extract was shown to reduce fascin and NF-B expression, as well as the activities of urokinase-type plasminogen activator, MMP-2, and uPA-9 synthesis, and to limit the migration and invasion of the highly metastatic MDA-MB231 cells [38]. When MCF-7 cells were treated to a red wine polyphenol fraction, it was discovered that the cells had membrane damage, decreased mitochondrial function, and G_2/M cell cycle arrest. When scientists searched for active substances in the Vitis amurensis grape, amurensin-G was shown to be the most potent inhibitor of VEGF production in tamoxifen-resistant MCF-7 cells. Pin1 inhibition resulted in the suppression of VEGF gene transcription. In MCF-7 cells, grape extract also inhibited Snail and phosphorylated signal transducers and activators of transcription-3, which reduced cell invasion, migration, and bone turnover [39].

Mango

Mango, a well-known tropical fruit, includes a number of polyphenolic compounds. Mango polyphenolics were found to be cytotoxic to BT474 cells *in vitro*; this resulted in a 73% reduction in tumor volume in mice bearing BT474 xenografts as compared to control animals. The PI3K/AKT pathway and MiR-126 both had a part in controlling these outcomes. Mango peel extract exhibited the greatest polyphenol content and dramatically increased cell death in MDA-MB-231 cells while inhibiting the viability of MCF-7 cells [40]. Mango seed ethanolic extract boosted pro-apoptotic proteins including Bax and Caspase-7/8/9 while decreasing anti-apoptotic proteins in MDA-MB-231 and MCF-7 cells. The effects of the medication were also revealed to be influenced by oxidative stress in

BC cells. Since mango gallotannins are not absorbed, their bioactivities are often not investigated. Gallotannins and mango polyphenols have both been demonstrated to inhibit the development of BC ductal carcinoma in situ *in vitro*, most likely by way of the AKT/mTOR signaling pathway [41].

Mangosteen

Popular fruit from the tropics is mangosteen. In SKBR3 cell lines, the pericarp crude methanolic extract may inhibit proliferation and encourage apoptosis. Significant cytotoxicities were also produced by the phenolics against MCF-7 cells. Mangosteen's pericarp is a strong source of anti-inflammatory, anti-cancer, and antioxidant compounds [42]. In SK-BR-3 BC cells, α-mangostin has shown dose-dependent anti-aromatase activity. Additionally, it was demonstrated that α-mangostin influences the HER2/PI3K/Akt and MAPK signaling pathways on T47D cells. α-Mangostin treatment resulted in alterations to the cell cycle and mitochondria-mediated cell death in MDA-MB231 cells [43]. In SKBR3 cells, mangosteen displayed apoptotic structures. In addition, α-mangostin induced apoptosis in human BC cells and lowered the expression and intracellular activity of the FAS enzyme. It was also shown that MCF-7 cells, which are ER-positive, are more susceptible to the effects of α-mangostin than MDA-MB-231 cells, which are ER-negative, and that ER knockdown decreased the suppression of cell growth and activation of caspase-7 by α-mangostin. Human BC cells exposed to β-mangostin undergo apoptosis and have their proliferation inhibited [44]. Metastasis to lymph nodes contributes to BC's lethality. α-Mangostin significantly increased survival rates in mice with breast cancers and significantly decreased tumor volume, as well as the rate of recurrence and circulation of lymph node metastases. *In vitro*, α-mangostin induced apoptosis, cell cycle arrest in the G/S phase, and decreased levels of phosphorylated Akt-threonine 308. When panaxanthone was given to mice, there was a significant decrease in the amount of lung and lymph node metastases as well as breast tumors. These negative effects were shown to be caused by an increase in apoptotic cell death, antiproliferation, and antiangiogenesis. It has been demonstrated that α-mangostin-induced apoptosis can cause BJMC3879 cells to die [45].

Pepper

Piperine is said to have anti-BC effects. Piperine reduced TNBC xenografts growth in immune-deficient mice and suppressed the proliferation, motility, and metastasis of TNBC cells *in vitro*. *In vitro* studies revealed that the BC cells overexpressing HER2 were cytotoxic and apoptotic, and that piperine inhibited their migration [46]. Piperine, which suppressed HER2 and FAS expression and downregulated the expression of AP-1 and NF-κβ, significantly decreased EGF-induced MMP-9 synthesis. In addition, the piperine inhibited $4T_1$ cells' ability to proliferate and, in a dose- and time-dependent way, induced apoptosis while activating caspase-3. Additionally, it prevented the growth of $4T_1$ tumors and significantly decreased lung metastasis *in vivo* by administering piperine [47].

Pomegranate

It has been discovered that pomegranate fruit contains a lot of polyphenols, especially ellagitannins, which have antioxidant and antiinflammatory properties. In MCF-7 cells treated with pomegranate extract, G_2/M cell cycle arrest and death were observed. Reduced homologous recombination may be responsible for the consequences, which may render cancer cells more susceptible to double strand breaks [48]. PE affected the DMBA-induced breast cancer in rats in a proapoptotic and antiproliferative manner, possibly by concurrently affecting the ER and Wnt/-catenin signaling pathways. Pomegranate seed oil that is hydrophilic drastically abridged the survival of MDA-MB-231 and MCF-7 cell lines and caused a cell cycle arrest in the G_0/G_1 phase. Pomegranate juice or its components combined with pomegranate juice may inhibit the metastatic activity of BC cells [49]. On BC cells, PE was shown to target microRNAs155. In MCF-7 cancer cells treated with pomegranate peel extract, the expression of the Bax and Bcl-2 genes rose, whereas the expression of both genes reduced in MCF-7 cancer cells [50]. The seed lipid extract included conjugated octadecatrienoic acids, but the aqueous extract contained elagannins and phenolic acids. The possibility of protecting estrogen-responsive BCs is further suggested by the fact that drugs derived from pomegranate ellagitannin suppress the activity of aromatase and the proliferation of BC cell lines. Pomegranate possesses adjuvant therapeutic potential and chemopreventive, as demonstrated by the polyphenols from fermented pomegranate juice and whole pomegranate seed oil that both inhibited the formation of malignant lesions brought on by DMBA in a murine mammary gland organ culture [51].

Saffron

Saffron is frequently used in recipes from the Mediterranean, Indian, and Chinese cuisines. Two bioactive substances present in saffron, crocin and crocetin, have been proven to have anticancer effects. Crocetin significantly reduced MDA-MB-231 cancer cells' ability to proliferate and invade, and the effect was linked to the MMP expression downregulation. N-methyl-N-nitrosourea-induced BC frequency in rats was decreased by crocin and crocetin. Crocetin is therefore more effective than crocin during both the initiation and promotion phases of chemoprevention [52,53].

Chemoprevention perspectives of dietary foods

Due to the severe side effects and rising rates of multidrug resistance, the existing BC treatment methods are becoming more ineffective. Because DFs have such strong anticancer potential,

utilizing a combined therapy strategy might be quite beneficial in this case [54]. DFs that change cancer-related pathways and restrict the formation of cancerous cells may lower the aggressiveness of BC. Food-derived items are especially intriguing for research termed as “chemopreventive agents” owing to their safety and lack of stigma as "medicine," and they may find broad, long-term usage in persons at normal risk. Phytochemicals may directly or indirectly affect certain molecular targets to exert their positive effects on health [55]. DFs have been used to make cancer chemotherapy drugs ethnobotanically. New substances now being investigated in nature may provide a variety of lead structures that may be used as templates to synthesise new, pharmacologically superior pharmaceuticals. Vegetables, fruits, herbs, and fermented plant products and extracts may contain naturally occurring anticancer compounds. These compounds' anticancer properties may be influenced by antioxidants, free-radical scavengers, and cell-based inhibitors of DNA-altering enzymes. When combined, these characteristics ought to offer defence against dangerous somatic mutations and epigenetic DNA alterations. Malignant cells must proliferate, receive energy, and create an angiogenic pathway in order to survive in tumor masses. By altering the genes that affect these pathways, tumor mass may be decreased and even reverted [56]. According to the World Health Organization, the majority of people continue to use traditional plant medicines for their basic healthcare, and 82% of plant-derived pharmaceuticals were connected to their initial ethnopharmacological research purpose. Traditional medical knowledge inspired resurgence in interest in medicinal plants as potential remedies, which in turn led to the discovery of several natural compounds that are today well-known medications. The possible synergistic properties of these extracts when combined with certain vehicles are thought to be caused by interactions between various target proteins, genes, and signalling cascades in conventional medicine [57].

The physiologically active substances contained in plants may be applied to treat a number of illnesses. Researchers have turned to DFs to develop inventive cancer analysis with least predicament because there aren't any commercially available medications with comparable negative effects. A number of researches conducted all over the world have demonstrated that DFs target a wide range of BC-related pathways, providing protective feedback against malignancies and likely playing a crucial role in BC prevention and therapy. When BC patients employ alternative and complementary medicine to assist managing their treatment-related symptoms and side effects, they may have a higher likelihood of survival and a better quality of life [58]. Effective treatments must be created in order to stop, delay, diminish, or even reverse the illness in women who are at high risk for BC. DFs perform better than synthetic ones in terms of toxicity and adverse effects when it comes to BC chemoprevention. In order to tackle the recurring phenomenon of resistance to hormonal and targeted treatments, which are now the standard of care, first-line treatment for BC patients requires novel, more potent, and less toxic medications. Epigallocatechin gallate, a polyphenolic substance found in green tea, resveratrol, a phytoalexin found in grapes, and omega-3 fatty acids from fish have all been demonstrated to have anti-cancer and chemopreventive qualities. Additionally, these substances have been extracted from fruit and plant medicines [59]. Alternative medicine and dietary approaches are being emphasized more and more in relation to the prevention and treatment of BC. It has been shown that a variety of DFs and bioactive ingredients included in food reduce BC development by reducing estrogen-induced oxidative damage and ER signaling. Numerous epidemiological studies have found a link between consuming more fruits and vegetables and a reduced risk of BC. In extensive experimental studies, it has been demonstrated that a variety of dietary DFs have an impact on the onset and progression of BC. They employ a number of mechanisms to fight BC, such as lowering ER-expression and activity, preventing the growth, migration, metastasis, and angiogenesis of breast tumor cells, inducing cell arrest and apoptosis, and increasing the sensitivity of cancer cells to radiation and chemotherapy [60].

CONCLUSION

BC prevention and treatment are major responsibilities of DFs. The majority of naturally occurring dietary compounds’ usage is widespread and has been practiced for a very long period in traditional civilizations. The development of these compounds as a treatment for treating BC patients must be given priority over efforts to enhance their activity. Since these natural compounds have the ability to influence several pathways, they can be used as a therapeutic system on their own or in conjunction with other therapies. Another justification for eating these foods is to avoid BC. They can function in a number of ways without triggering any kind of risky reaction. This study focuses on a wide variety of natural compounds, looking at their mode of action, distribution, interactions, and future research potential. More research is required to ascertain these chemicals correct participation in the process since they could be crucial in BC therapy and prevention.

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