OPEN ACCESS

Phytopharmacological Communications

DOI: doi.org/10.55627/ppc.004.002.0911

Review Article

Promising Phytochemicals in Fight Against Breast Cancer; A Narrative Review

Huzaifa Shoaib* and Arfa Khan

Shifa College of Pharmaceutical Sciences, Shifa Tameer-e-Millat University, Islamabad, Pakistan.
**Correspondence:* Huzaifa Shoaib: huzaifashoaib137@gmail.com

Abstract

Breast cancer is the most prevailing cancer affecting women worldwide. This study includes a review of the genetic, molecular, and environmental factors that contribute to breast cancer pathogenesis and its progression including various genes, such as the BRCA-1 and BRCA-2 that are critical in repairing DNA as well as in hereditary breast cancer. We have also reviewed HER-2-positive breast cancer, and also further examined the oncogenic role the Ras and BRAF proteins play in breast cancer pathogenesis and treatment. Despite the conventional therapies being helpful, challenges remain such as tumor relapse and tumor metastasis, which is why alternative novel ways have to be invented for treatment. Several plant-based compounds known as phytochemicals are anticancer agents and are examined in detail in this review. They include Curcumin, EGCG, Genistein, Apigenin, Quercetin and Berberine. These compounds are discussed for properties such as inhibiting cell proliferation in cancers, modulating key molecular pathways, and inducing cell apoptosis. This review also elaborates on challenges faced in the clinical application of phytochemicals, shedding light on their bioavailability issues and drug-drug interactions. We propose that these compounds might work alongside current breast cancer treatments, especially for resistant and relapse cases.

Keywords: Breast Cancer; Phytochemicals; Curcumin; Quercetin; Metastasis; Plant-based compounds

1. Introduction

Breast cancer is the most frequently diagnosed cancer among women and the leading cause of cancer-related deaths worldwide. There were an estimated 670,000 deaths from breast cancer globally in 2022 (Organization 2024). In 2023, about 43,700 deaths from invasive breast cancer were predicted in the United States, accounting for about 30% of female cancers (Clancy and News 2023). Breast cancer patients make up to 36% of oncological cases (Nardin et al. 2020, Cuthrell and Tzenios 2023). According to the World Health Organization (WHO), breast cancer was the most frequently diagnosed cancer among women in 157 out of 185 countries in 2022, reflecting its global prevalence (Organization 2023).

Breast cancer primarily affects middle-aged and older women, with an average of diagnosis being 62 years. About half of women diagnosed are 62 years or younger, while only a small percent are younger than 45 years (Pilleron *et al*. 2019, Song *et al*. 2014). The lifetime risk of developing invasive breast cancer is 1 in 8, and the probability of death is about 1 in 36 (Society 2023). Although breast cancer rates have been reduced due to advancements in treatment and its early detection, over 4 million survivors are currently present in the United States (Society 2023).

Breast cancer can be classified based on its dependency on estrogen signaling into estrogen-dependent and estrogen-independent types. Estrogen-dependent breast cancers rely on estrogen for growth and proliferation while estrogen-independent breast cancers grow regardless of estrogen signaling (Torres-Arzayus *et al*. 2010). The causes of

breast cancer are due to several factors such as genetic, environmental, and lifestyle factors. Lifestyle-related risks include poor dietary choices and lack of exercise. 10% of breast cancer cases are hereditary involving mutation in genes such as *BRCA1* (Breast Cancer Gene 1) and *BRCA2* (Breast Cancer Gene 2) (Institute 2024). The remaining 90% are attributed to sporadic genetic mutations, that often arise from unknown factors (Walsh *et al*. 2020).

Mutations in *BRCA1* and *BRCA2* are associated with an increased risk of early-onset breast cancer. They account for about 90% of hereditary cases (Kwong *et al*. 2011, Calderón-Garcidueñas *et al*. 2005, Chen *et al*. 2009, Malone *et al*. 2006, Martin *et al*. 2009). These tumor suppressor genes encode tumor suppressor proteins that regulate cell growth and maintain genomic stability by repairing damaged DNA. Tumor suppressor genes function as 'brakes' to prevent uncontrolled cell division. When these genes are mutated, they impair the ability to repair DNA damage, leading to genomic instability and ultimately, cancer progression (Motoyama and Naka 2004).

Clinical manifestations of breast cancer vary, but its early stages are usually asymptomatic. Symptoms include the presence of a lump, changes in breast sizes or shape, nipple discharge or skin changes such as red or scaly skin (Berman 2000). The risk factors of breast cancer include advanced age, dense breast tissue, genetic predispositions, and prolonged exposure to estrogen due to late menopause or reproductive history (Feng *et al*. 2018). The standard treatments include chemotherapy, surgery, radiation, and targeted therapies such as anti-estrogens (e.g. Tamoxifen) or aromatase inhibitors (e.g. Anastrozole) (Israel *et al*. 2018). However, these approaches usually face certain limitations including tumor relapse and metastasis. Recent interest in the therapeutic potential of naturally occurring plant extracts and phytochemicals (Imran et al. 2012, Hussain et al. 2009) as alternatives to conventional treatments is yielding hope that such a strategy might be useful for treating cancers. The compounds are derived from plants and have shown efficiency in targeting estrogen-dependent and estrogen-independent breast cancer cells as well as breast cancer stem cells (Israel *et al*. 2018).

This review aims to summarize the therapeutic effect of phytochemicals in the prevention and treatment of breast cancer, emphasizing their potential to enhance therapeutic outcomes with minimal toxicity. It also highlights the efficacy of phytochemicals in fighting breast cancer by addressing its pathophysiological effects and pharmacotherapeutic goals. Furthermore, the review focuses on the role of Complementary and Alternative Medicine (CAM) as a safer and effective treatment strategy. By presenting these insights, this review aims to inspire scientists to develop phytochemical-based treatment options for breast cancer patients, along with reducing the risk of associated disorders.

2. Pathophysiological Insights of Breast Cancer

The breast tissue is composed of lobules, lobes, and ducts that play a vital role in the production and transport of milk. Each breast consists of 15-20 lobes, which divide further into lobules that end in milk-producing bulbs. These tissues are connected with each other through ducts, facilitating milk flow. The breasts are also supported by blood vessels and lymphatic vessels. The lymphatic system is vital for providing immune defense, by housing white blood cells which fight against infections and diseases (Sharma *et al.* 2021).

Breast cancer primarily begins because of genetic mutations which affect tumor suppressor genes such as *BRCA1* and *BRCA2*. These genes are essential for the repair of double-stranded DNA breaks through homologous recombination. Mutations in these genes obstruct DNA repair, which leads to error-prone pathways such as non-homologous end-joining (Narod and Salmena 2011). This causes mutations and chromosomal rearrangements. In some cases, it leads to mutant cells with increased proliferative and metastatic properties, which are the hallmarks of cancer *(Fares et al*. 2020). *BRCA1* also regulates the cell cycle, where it

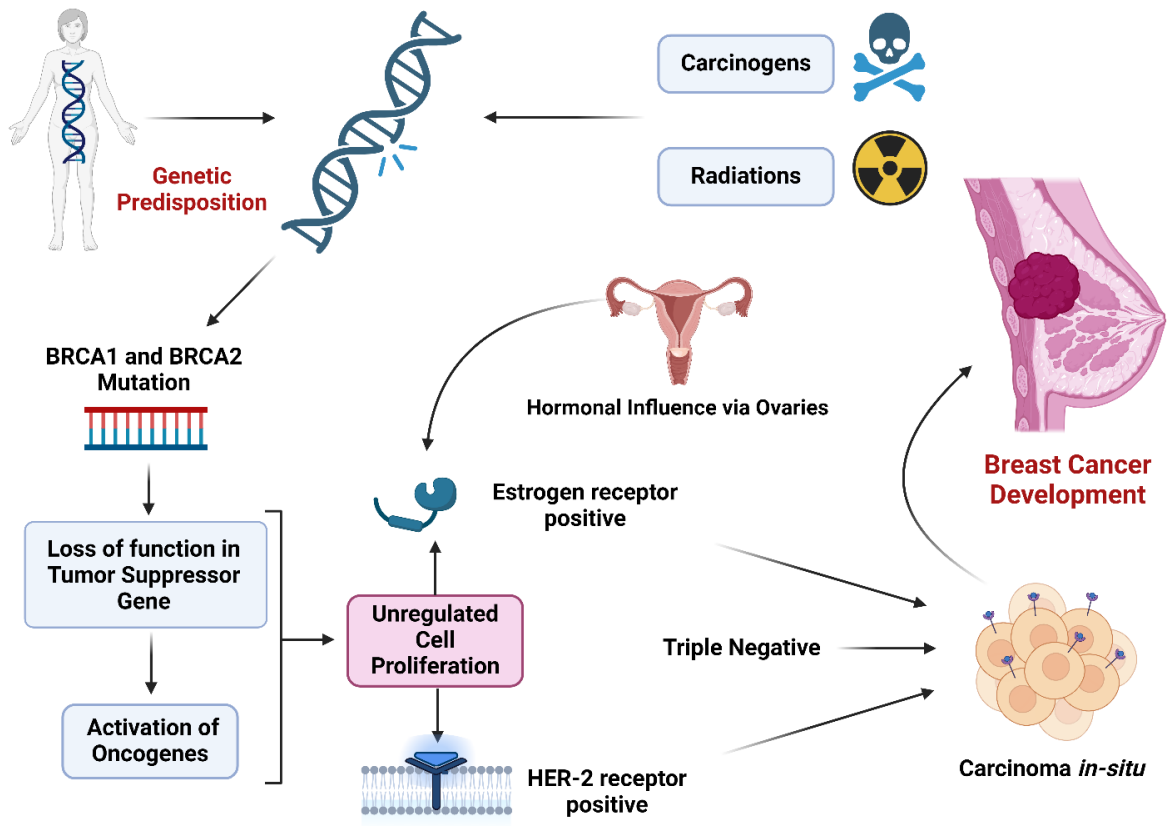

Figure 1. Pathogenesis of Breast cancer

ensures arrest at the S or G2/M phases in response to DNA damage. Its activation depends on phosphorylation by ATM (Ataxia Telangiectasia Mutated) (Xu *et al.* 2001). More than half of *BRCA1* - associated tumors lead to invasive ductal carcinomas (Lakhani *et al.* 2005).

An additional pivotal factor in breast cancer is the HER2 (Human Epidermal Growth Factor Receptor 2) protein. It is encoded by the *erbB-2* gene. HER2 is a receptor tyrosine-protein kinase, which aids the normal growth and proliferation of breast cells. However, abnormal overexpression of this oncogene results in HER2-positive (HER2+) breast cancers. These are more likely to metastasize and exhibit rapid growth. (Asif *et al.* 2016). The pathophysiological insights of breast cancer are illustrated in Figure 1.

The Ras pathway also plays a vital role in breast cancer. Overexpression of oncogenic H-Ras stimulates cell cycle re-entry from the G0 phase without depending on growth factors, while also altering growth factor receptor expression to further cause (Cox and Der 2010). Another oncogene in the pathway, the *BRAF* gene encodes a serine-threonine kinase that regulates the mitogen-activated protein kinase (MAPK) pathway. Mutations in *BRAF*, especially at codon 600 (V600E) lead to uncontrolled cell proliferation and oncogenic transformation (Wang *et al.* 2022).

Hormone replacement therapy (HRT) which is often prescribed to reduce menopausal symptoms, has been associated with an increased risk of breast cancer, specifically estrogen receptor-positive types. Combination therapies of estrogen and progesterone lead to a higher risk as compared to estrogen-only therapies (Narod 2011).

3. Anti-Cancer Role of Phytochemicals

Several natural and synthetic compounds show useful pharmacological actions (Hansraj et al. 2003, Aslam et al. 2008, Gul et al. 2011, Ahmed et al. 2014). Phytochemicals are bioactive compounds derived from plants that are being studied in detail for their health-promoting properties, including anti-cancer effects (Dillard, German, and Agriculture 2000). Studies based on epidemiology highlight the protective role of diets rich in fruits and vegetables against cancer. Phytochemicals act at different stages of carcinogenesis by enhancing the detoxification of carcinogens, suppressing inflammation, (e.g. cyclooxygenase-2 inhibition) blocking cell division, and inducing apoptotic in cancer cells (Johnson 2007).

4. Promising Phytochemicals for Breast Cancer

4.1 Curcumin

Curcumin is a yellow pigment extracted from the rhizome of *Curcuma longa* (turmeric). It is broadly studied for its anti-cancer properties, specifically in breast cancer. (Cridge, Larsen, and Rosengren 2013). It displays anti-oxidant, anti-proliferative, and apoptotic effects by regulating various molecular targets, such as inflammatory cytokines, transcription factors, and gene products associated with cell proliferation and survival.

Curcumin has been shown to suppress tumor growth in animal models, such as xenotransplant and orthotransplant systems, either in combination with chemotherapeutic agents or radiation or used alone (Kunnumakkara, Anand, and Aggarwal 2008). For example, it induces cell-cycle arrest in the G2/M phase, activates mitotic checkpoints, and blocks cell proliferation by suppressing microtubule dynamics in the MCF-7 breast cancer cell lines (Banerjee, Singh, and Panda 2010). Additionally, curcumin downregulates the expression of EZH2 (Enhancer of Zeste Homolog 2) and regulates the MAPK (Mitogen-Activated Protein Kinase) signaling pathway by activating JNK (c-Jun NH2-terminal kinase), ERK (Extracellular Signal-regulated Kinase) and p38 kinase, which results in improved apoptosis and inhibition of tumor growth (Hua *et al.* 2010).

One mechanism involves the regulation of the Wnt/β-catenin signaling pathway, which plays a pivotal role in breast cancer progression. Curcumin suppresses β-catenin and cyclin D1 expression in MCF-7 and MDA-MB-231 cells, effectively stopping cancer progression (Prasad *et al.* 2009). Additionally, curcumin enhances the expression of the Maspin gene, a serine protease inhibitor that inhibits tumor cell motility and invasion. This effect is followed by the upregulation of tumor suppressor protein p53 and the downregulation of anti-apoptotic protein Bcl-2 (Prasad *et al*. 2010).

In HER2-positive breast cancer, the HER2 oncoprotein is overexpressed. Curcumin reduces HER2 protein levels, suppresses Akt and MAPK phosphorylation, and inhibits NF-κB activity in BT-474 and SK-BR-3-hr cells (Lai *et al*. 2012). By targeting NF-κB signaling, curcumin enhances the efficacy of chemotherapy by improving p53-p300 cross-talk (Sen *et al.* 2011).

Curcumin also inhibits angiogenesis by downregulating VEGF expression which is a key mediator of blood vessel formation in tumors. This anti-angiogenic effect is shown in studies involving osteopontin and medroxyprogesterone acetate-induced VEGF expression (Chakraborty *et al.* 2008, Carroll, Ellersieck, and Hyder 2008). Furthermore, curcumin has been shown to act synergistically with chemotherapeutic agents like Mytomycin C (MMC), enhancing its anti-proliferative effects via the p38 MAPK pathway while reducing toxicities related to MMC *(Zhou et al. 2009, Zhou et al.* 2011).

4.2. Epigallocatechin gallate (EGCG)

Epigallocatechin gallate (EGCC) is a green tea polyphenol that has the potential to have an impact on diversified biological pathways, such as in gene expression, growth factor-mediated pathways, the mitogen-activated protein kinase-dependent pathway, and the ubiquitin-

Table 1. Some possible anti-breast cancer molecular mechanisms for genistein and its targets.

EFFECT	PROTEINS/PATHWAYS AFFECTED	REFERENCES
Anti-proliferative effects	Upregulation of ATM Upregulation of APC Upregulation of SERPINB5 Downregulation of DNA methylation Upregulation of ER α Decreased ER binding Erβ inhibited E2-dependent cell growth	(Xie *et al*. 2014, Liu *et al.* 2019, Li *et al.* 2013, Mukund 2020, He, Chen, and wellness 2013)
Epigenetic Modifications	Tumor suppressors p21 and p16 c-MYC-BMI complexes Regulation of E2-induced genes	(He, Chen, and Wellness 2013)
Induction of Apoptosis	Downregulation of CIP2A mRNA. modulation of E2F1 Activation of PPPA Inactivation of NF-kB Bcl-2 Bax Activation of Caspase-3 Upregulation of DNA fragmentation	(Zhao *et al.* 2016, He, Chen, and Wellness 2013, Hsieh *et al.* 1998)
Arrest of cell cycle	G0/G1 arrest by cell cycle transition G2/M phase arrest via cyclin B	(Jiang *et al*. 2018, Kobayashi, Nakata, and Kuzumaki 2002)
Decreased response to growth factors	Downregulation of tyrosine kinase activity Expression of SRF mRNA	(Chen *et al*. 2003, Yan *et al.* 2010)

proteasome degradation pathway. Identifying and further characterizing the molecular targets of EGCG will improve understanding of the underlying mechanisms of its anti-carcinogenic and cancer-defensive activities (Chen *et al.* 2011).

Studies have displayed that EGCG substantially constrained MCF-7 cell growth in a time- and dose-dependent manner. EGCG induced apoptosis and disorganized cell cycle advancement at the G2-M phase, as reported in flow cytometry analysis. Furthermore, EGCG elevated PARP procaspase-3 and procaspase-9 at the protein level and inhibited miR-25 expression. Reclamation of miR-25 in repressed EGCG-induced cell apoptosis. Immunohistochemistry staining determined that EGCG suppressed tumor development *in vivo* by down-regulating the expression of miR-25 and proteins associated with apoptosis, this was additionally verified by a decline of Ki-67 and elevation in pro-apoptotic PARP expression (Zan *et al.* 2019). EGCG is efficient against radiation-induced dermatitis in breast cancer patients.

A single-arm trial was held to test the supposition that topical EGCG is competent against radiation-induced dermatitis in 49 breast cancer patients undergoing radiotherapy after mastectomy. The results showed that topical EGCG reduced symptoms of radiation-induced dermatitis, including pain, burning, tenderness, pulling, and itching in patients undergoing radiotherapy with minimal toxicity and no severe cases reported (Zhu *et al.* 2016).

4.3. Genistein

Genistein, a synthetic phytoestrogen found in soybeans, is an isoflavone native to Southeast Asia. It was first confined from *Genista tinctoria (L.)* and was titled after it. Subsequent to this, it has often been determined in the Trifolium spp., exclusive to the Leguminosae (Fabaceae) (Dixon and Ferreira 2002).

According to epidemiological evidence, it has been implied that soy consumption is inversely proportional to breast cancer risk. Asian men and women who consumed a soy diet had a 40% diminished predominance of mammary cancer. On the other hand, Asians who did not consume a soy-rich diet were deprived of this preservation (Wu *et al.* 2004, Dai *et al.* 2001). Genistein has been associated with distinct pathways and targets. Cell division cycle modification, anti-cell proliferation, and apoptosis are a few of the approaches that have been projected as genistein targets and pathways for anti-breast cancer tumorigenesis (Bhat *et al.* 2021).

SRF—Serum Response Factor; CIP2A—cancerous inhibitor of PP2A; E2F1—Transcription factor E2F1; PPPA— PP2C-family protein phosphatase; NF-kB—nuclear factor kappa-light-chain-enhancer of activated B cells; Bcl-2 Bax- BCL2-associated X protein; ATM—ataxia telangiectasia mutated; APC—Adenomatous Polyposis Coli; SERPINB5—Serpin Family B Member 5; ER—Estrogen Receptor; PTEN—Phosphatase and Tensin Homolog; PAK2- Serine/threonine-protein kinase PAK 2; c-MYC-BMI—myc and bmi-1 oncogenes; E2- 17β-estradiol.

Several clinical trials have explored the use of genistein in breast cancer treatment. These trials investigate its safety, efficacy, and effect on different biomarkers in breast cancer patients (Medicine 2025).

4.4. Apigenin

Apigenin, an acclaimed flavonoid is found in considerable dietary plant foods including chamomile, lemon balm, oranges, celery, parsley, and celeriac. Comprehensive studies have concluded that apigenin has antioxidant, anti-carcinogenic, and anti-inflammatory properties (Mohammad Nabavi *et al.* 2015).

A study examined the cellular mechanisms that were lying the induction of cell cycle arrest by apigenin. The results showed that apigenin at the non-apoptotic induction concentration suppressed cell proliferation and promoted cell cycle arrest at the G2/M phase in the MDA-MB-231 breast cancer cell line (Tseng *et al.* 2017).

A study showed that apigenin functions as both an estrogen and anti-estrogen in a dose-dependent manner. At low concentrations, apigenin stimulated the growth of MCF-7 cells, however at higher concentrations, it inhibited their growth. When used in combination with either Tamoxifen or Fulvestrant, apigenin showed synergistic and growth-inhibitory effects on both antiestrogen-sensitive and –resistant breast cancer cells (Long *et al.* 2008).

4.5. Quercetin

Quercetin is an ample plant-derived flavonoid in vegetables and fruits such as apples, legumes, green tea, berries, citrus fruits, parsley, onions, and red wine *(Chirumbolo and Targets 2010, Li et al.* 2016). According to *in-vivo* and *in-vitro* studies, quercetin enforced its anticancer properties by the regulation of certain specific signaling pathways consisting of reduction of oncogene expression (Ranganathan, Halagowder, and Sivasithambaram 2015), apoptosis of malignant cells, and reducing the tumor volume (Hashemzaei *et al.* 2017, Yang, Liu, and chemistry 2009), regulation of the cell cycle (Priyadarsini *et al*. 2010) and inhibition of angiogenesis (Pratheeshkumar *et al.* 2012).

In a study, quercetin was found to inhibit growth in MCF-7 breast cancer cells by inducing cell cycle arrest at the G2/M phase and promoting apoptosis. This treatment led to temporary accumulation of cells in the M phase, increased cyclin B1 and Cdc2 kinase activity, and elevated p21CIP1/WAF1 protein levels. These findings suggest that quercetin inhibits cell growth through both apoptosis induction and cell cycle suppression. (Choi *et al.* 2001).

4.6. Berberine

Berberine is found in plants such as Berberis e.g. Oregon grape, barberry, tree turmeric, yellow root, and Chinese goldthread. It is a quaternary ammonium salt from the protoberberine group of

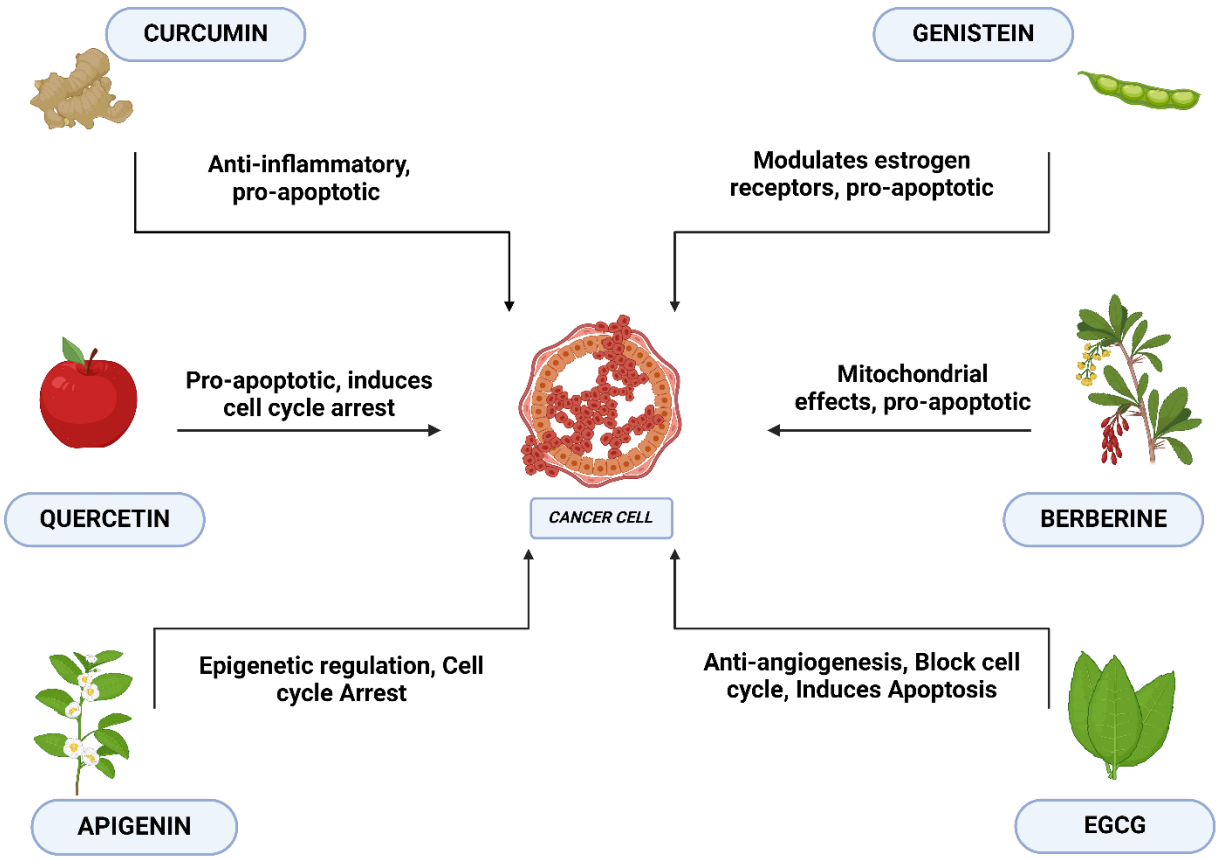

Figure 2. A representation of phytochemicals and their anti-cancer properties including their mode of action through which they exhibit antitumor effects.

isoquinoline alkaloids (Cicero, Baggioni, and diseases 2016).

In a study, purified berberine was tested against breast cancer (MCF-7) and normal human breast epithelial (MCF-12F) cells for 24, 48, and 72 hours at different concentrations. Using MTT assay, a colorimetric technique used to assess cell viability and cytotoxicity by measuring mitochondrial activity, berberine demonstrated significant cytotoxic effects on MCF-7 cells while excluding normal epithelial cells. In accordance with these findings, further experiments were conducted to explore the mechanism of action of berberine. MCF-7 cells were treated with berberine for 48 and 72 hours, which resulted in apoptosis induction, as shown through cell cycle arrest and DNA fragmentation using agarose gel electrophoresis. Additionally, immunoblotting analysis showed that berberine exerts a pro-apoptotic effect by activating mitochondrial and caspase-dependent apoptotic pathways. These results suggest that berberine suppresses the proliferation of MCF-7 breast cancer cells and highlights its potential as a naturally occurring compound for breast cancer therapy (Patil, Kim, and Jayaprakasha 2010).

Hence, the phytochemicals such as curcumin, epigallocatechin-3-gallate (EGCG), genistein, apigenin, quercetin, and berberine exhibit significant potential in targeting molecular pathways involved in cancer development and regulation of the cell cycle. Curcumin, a natural compound from turmeric, interferes with signaling pathways like NF-κB, PI3K/AKT, and MAP-Kinase, reducing cancer cell proliferation and promoting apoptosis while halting cell cycle progression at critical checkpoints. EGCG, the

active component in green tea, modulates pathways such as STAT3, Wnt/β-catenin, and ERK, inducing cell cycle arrest and enhancing programmed cell death. Genistein, a soy-derived isoflavone, interacts with estrogen receptors and key pathways like PI3K/AKT and NF-κB, disrupting cancer cell growth and regulating the cell cycle at the G2/M phase. Apigenin, a flavonoid abundant in fruits and vegetables, inhibits COX-2 and STAT3 signaling, causing cell cycle arrest at the G1 phase and reducing inflammation-driven cancer progression. Quercetin, another potent flavonoid, targets p53, MAPK, and PI3K/AKT pathways, arresting the cell cycle and inducing apoptosis while impairing angiogenesis. Berberine, an alkaloid from medicinal plants, influences AMPK, mTOR, and NF-κB pathways, effectively halting cell cycle progression and suppressing tumor growth. Together, these phytochemicals offer a promising, natural approach to disrupting the intricate molecular pathways and cell cycle mechanisms that drive cancer progression (Abotaleb *et al.* 2019, Rahman *et al.* 2022).

5. Opportunities and Challenges

Various phytochemicals have been thoroughly searched for their potential to prevent and treat cancer. These compounds are studied with the goal of introducing them as anticancer agents. However, the application of phytochemicals in cancer treatment comes with certain challenges. Although their chemical structures are fully understood, further study is required to extensively understand their physicochemical properties, which can affect their efficiency (Bishayee and Sethi 2016).

One major challenge is their bioavailability. Due to the low bioavailability of many phytochemicals, their efficiency is limited. This issue has been addressed by nanotechnology. It helps to improve the effectiveness and absorption of these compounds. Techniques such as micelles, phospholipid complexes, and liposomes are used to improve the water solubility of these compounds, thereby increasing their bioavailability (Aqil *et al.* 2013).

Generally, phytochemicals are considered non-toxic, however, there are cases where they show toxic effects, especially in combination with other drugs (e.g. drug-drug interactions). This drawback has reduced their impact and use in cancer-related therapies. Moreover, because they are natural compounds, they tend to have synergistic effects when consumed in whole plant forms, rather than as purified and isolated extracts (Ayaz *et al.* 2022). Improvements and advancements in technology may enable these compounds to be considered as effective agents in cancer treatment. By improving formulation and delivery, it is becoming highly possible to develop phytochemicals as a suitable option for preventing cancer (Gupta, Singh, and Sharma 2017). However, there are concerns about the long-term effects of phytochemicals. Because of their inconsistent bioavailability and dosage levels, further elaborate research is required to understand their safety, effectiveness, and side effects over prolonged use. This lack of data on their long-term outcomes remains an ongoing investigation (Choudhari *et al.* 2020).

6. Conclusion and Future Prospects

Various mechanisms have been used by phytochemicals to suppress breast cancer growth such as apoptosis induction, modulation of signaling pathways, and tumor growth inhibition. Phytochemicals have exhibited adequate potential in diminishing breast cancer through these diverse mechanisms. The most recent research body demonstrates that compounds like flavonoids, alkaloids, and polyphenols are effective in targeting different aspects of breast cancer pathogenesis. However, challenges arise with taking these findings from the laboratory to standardize treatment. This is due to phytochemicals exhibiting inconsistent bioavailability, dosage levels, and long-term effects call for further research. Phytochemicals can be improved in their therapeutic abilities through enhanced delivery systems for drugs, personalized medicine approaches, and combination

therapies that use current anti-cancer agents. In addition to these clinical trials on a large scale are necessary to ensure the safety and efficacy of phytochemicals among different populations. The combination of traditional and common cancer treatments with phytochemicals may lend a helping hand to more broad patterns and therefore enhance management strategies for breast cancer patients leading to enhanced health outcomes eventually. Still, continued research is necessary to overcome the current shortcomings and limitations. This will ultimately enable researchers to fully utilize the potential of phytochemicals against breast cancer.

Competing Interests

The authors declare no competing interests.

Funding

No funding was received to assist with the preparation of this manuscript.

Ethics Approval

Not applicable, since the work does not involve any study with human participants or animals.

Consent Forms

Not Applicable

Author Contributions

H.S. conceived the study; H.S. and A.K. drafted the manuscript. All authors read and approved the final manuscript.

Acknowledgments

The authors thank Shifa Tameer-e-Millat University for providing an excellent environment for carrying out this scholarly work.

References

Abotaleb, Mariam, Samson Mathews Samuel, Elizabeth Varghese, Sharon Varghese, Peter Kubatka, Alena Liskova, and Dietrich Büsselberg. 2019. "Flavonoids in Cancer and Apoptosis." 11 (1):28.

Ahmed, Sagheer, Saima Gul, Fazean Idris, Abrar Hussain, Muhammad Zia-Ul-Haq, Hawa Z. E. Jaafar, and Marius Moga. 2014. "Anti-Inflammatory and Antiplatelet Activities of Plasma Are Conserved Across Twelve Mammalian Species." *Molecules* 19 (8):11385-11394.

Aqil, Farrukh, Radha Munagala, Jeyaprakash Jeyabalan, and Manicka V Vadhanam. 2013. "Bioavailability of phytochemicals and its enhancement by drug delivery systems." *Cancer letters* 334 (1):133-141.

Asif, Hafiz Muhammad, Sabira Sultana, Saeed Ahmed, Naheed Akhtar, and Muhammad %J Asian Pacific Journal of Cancer Prevention Tariq. 2016. "HER-2 positive breast cancer-a mini-review." 17 (4):1609-1615.

Aslam, Rukhsana, Sheikh A Saeed, Sagheer Ahmed, and John D Connor. 2008. "Lipoproteins inhibit platelet aggregation and arachidonic acid metabolism in experimental hypercholesterolaemia." *Clinical & Experimental Pharmacology & Physiology* 35.

Ayaz, Muhammad, Asif Nawaz, Sajjad Ahmad, Osama F Mosa, Alashary Adam Eisa Hamdoon, Modawy Alnour Khalifa, Abdul Sadiq, Farhat Ullah, Abdul Wadood, and Atul Kabra. 2022. "Underlying anticancer mechanisms and synergistic combinations of phytochemicals with cancer chemotherapeutics: potential benefits and risks." *Journal of Food Quality* 2022 (1):1189034.

Banerjee, Mithu, Parminder Singh, and Dulal %J The FEBS journal Panda. 2010. "Curcumin suppresses the dynamic instability of microtubules, activates the mitotic checkpoint and induces apoptosis in MCF-7 cells." 277 (16):3437-3448.

Berman, Joel A. 2000. *Comprehensive breast care and surviving breast cancer*: Branden Books.

Bhat, Smitha S, Shashanka K Prasad, Chandan Shivamallu, Kollur Shiva Prasad, Asad Syed, Pruthvish Reddy, Charley A Cull, and Raghavendra G %J Current Issues in

Molecular Biology Amachawadi. 2021. "Genistein: a potent anti-breast cancer agent." 43 (3):1502-1517.

Bishayee, A., and G. Sethi. 2016. "Bioactive natural products in cancer prevention and therapy: Progress and promise." *Semin Cancer Biol* 40-41:1-3. doi: 10.1016/j.semcancer.2016.08.006.

Calderón-Garcidueñas, Ana Laura, Pablo Ruiz-Flores, Ricardo M Cerda-Flores, and Hugo A %J Salud publica de Mexico Barrera-Saldaña. 2005. "Clinical follow up of Mexican women with early onset of breast cancer and mutations in the BRCA1 and BRCA2 genes." 47 (2):110-115.

Carroll, C. E., M. R. Ellersieck, and S. M. Hyder. 2008. "Curcumin inhibits MPA-induced secretion of VEGF from T47-D human breast cancer cells." *Menopause* 15 (3):570-4. doi: 10.1097/gme.0b013e31814fae5d.

Chakraborty, G., S. Jain, S. Kale, R. Raja, S. Kumar, R. Mishra, and G. C. Kundu. 2008. "Curcumin suppresses breast tumor angiogenesis by abrogating osteopontin-induced VEGF expression." *Mol Med Rep* 1 (5):641-6. doi: 10.3892/mmr_00000005.

Chen, D., S. B. Wan, H. Yang, J. Yuan, T. H. Chan, and Q. P. Dou. 2011. "EGCG, green tea polyphenols and their synthetic analogs and prodrugs for human cancer prevention and treatment." *Adv Clin Chem* 53:155-77. doi: 10.1016/b978-0-12-385855-9.00007-2.

Chen, Weiqiu, Kaifeng Pan, Tao Ouyang, Jinfeng Li, Tianfeng Wang, Zhaoqing Fan, Tie Fan, Benyao Lin, Youyong Lu, Weicheng %J Breast cancer research You, and treatment. 2009. "BRCA1 germline mutations and tumor characteristics in Chinese women with familial or early-onset breast cancer." 117:55-60.

Chen, Wen-Fang, Ming-Hui Huang, Chi-Hung Tzang, Mengsu Yang, and Man-Sau %J Biochimica et Biophysica Acta -Molecular Basis of Disease Wong. 2003. "Inhibitory actions of genistein in human breast cancer (MCF-7) cells." 1638 (2):187-196.

Chirumbolo, Salvatore %J Inflammation, and Allergy-Drug Targets. 2010. "The role of quercetin, flavonols and flavones in modulating inflammatory cell function." 9 (4):263-285.

Choi, Jung-A, Ja-Young Kim, Jeong-Yim Lee, Chang-Mo Kang, Ho-Jeong Kwon, Young-Do Yoo, Tae-Whan Kim, Yun-Sil Lee, and Su-Jae %J International journal of oncology Lee. 2001. "Induction of cell cycle arrest and apoptosis in human breast cancer cells by quercetin." 19 (4):837-844.

Choudhari, Amit S, Pallavi C Mandave, Manasi Deshpande, Prabhakar Ranjekar, and Om Prakash. 2020. "Phytochemicals in cancer treatment: From preclinical studies to clinical practice." *Frontiers in pharmacology* 10:1614.

Cicero, Arrigo FG, Alessandra %J Anti-inflammatory nutraceuticals Baggioni, and chronic diseases. 2016. "Berberine and its role in chronic disease."27-45.

Clancy, Erin %J Renal, and Urology News. 2023. "ACS Report Shows Prostate Cancer on the Rise, Cervical Cancer on the Decline."NA-NA.

Cox, Adrienne D, and Channing J Der. 2010. "Ras history: The saga continues." *Small GTPases* 1 (1):2-27.

Cridge, Belinda J, Lesley Larsen, and Rhonda J Rosengren. 2013. "Oncology Discovery."

Cuthrell, Kimberly Morton, and Nikolaos %J International Research Journal of Oncology Tzenios. 2023. "Breast Cancer: Updated and Deep Insights." 6 (1):104-118.

Dai, Q, XO Shu, F Jin, JD Potter, LH Kushi, J Teas, YT Gao, and W %J British journal of cancer Zheng. 2001. "Population-based case–control study of soyfood intake and breast cancer risk in Shanghai." 85 (3):372-378.

Dillard, Cora J, J Bruce %J Journal of the Science of Food German, and Agriculture. 2000.

"Phytochemicals: nutraceuticals and human health." 80 (12):1744-1756.

Dixon, R. A., and D. Ferreira. 2002. "Genistein." *Phytochemistry* 60 (3):205-11. doi: 10.1016/s0031-9422(02)00116-4.

Fares, Jawad, Mohamad Y Fares, Hussein H Khachfe, Hamza A Salhab, and Youssef Fares. 2020. "Molecular principles of metastasis: a hallmark of cancer revisited." *Signal transduction and targeted therapy* 5 (1):28.

Feng, Yixiao, Mia Spezia, Shifeng Huang, Chengfu Yuan, Zongyue Zeng, Linghuan Zhang, Xiaojuan Ji, Wei Liu, Bo Huang, Wenping %J Genes Luo, and diseases. 2018. "Breast cancer development and progression: Risk factors, cancer stem cells, signaling pathways, genomics, and molecular pathogenesis." 5 (2):77-106.

Gul, Saima, Sagheer Ahmed, Humaira Gul, and KF Kaneez. 2011. "Investigating the protective effect of Solanum melongena." *Asian J Health* 1 (1):276-294.

Gupta, Vivek Kumar, Reetika Singh, and Bechan %J Biochemical Compounds Sharma. 2017. "Phytochemicals mediated signalling pathways and their implications in cancer chemotherapy: Challenges and opportunities in phytochemicals based drug development: A review." 5 (1):1-5.

Hansraj, Natasha Imtiaz, Asma Mushir Ahmad Khan, Ameer Zaigham Rasheed, Abdul Mueed Zafar, Muhammad Ameen Rauf, and Sagheer Ahmad. 2003. "The inhibition of prostaglandin biosynthesis by human plasma and its relationship to albumin and haptoglobin." *Journal of Biological Sciences* 3 (12):1188-1202.

Hashemzaei, Mahmoud, Amin Delarami Far, Arezoo Yari, Reza Entezari Heravi, Kaveh Tabrizian, Seyed Mohammad Taghdisi, Sarvenaz Ekhtiari Sadegh, Konstantinos Tsarouhas, Dimitrios Kouretas, and George %J Oncology reports Tzanakakis. 2017. "Anticancer and apoptosis-inducing effects of quercetin in vitro and in vivo." 38 (2):819-828.

He, Fen-Jin, Jin-Qiang %J Food science Chen, and human wellness. 2013. "Consumption of soybean, soy foods, soy isoflavones and breast cancer incidence: Differences between Chinese women and women in Western countries and possible mechanisms." 2 (3-4):146-161.

Hsieh, Ching-Yi, Ross C Santell, Sandra Z Haslam, and William G %J Cancer research Helferich. 1998. "Estrogenic effects of genistein on the growth of estrogen receptor-positive human breast cancer (MCF-7) cells in vitro and in vivo." 58 (17):3833-3838.

Hua, Wen-Feng, Yong-Shui Fu, Yi-Ji Liao, Wen-Jie Xia, Yang-Chao Chen, Yi-Xin Zeng, Hsiang-Fu Kung, and Dan %J European journal of pharmacology Xie. 2010. "Curcumin induces down-regulation of EZH2 expression through the MAPK pathway in MDA-MB-435 human breast cancer cells." 637 (1-3):16-21.

Hussain, Javid, Nargis Jamila, Syed Abdullah Gilani, Ghulam Abbas, and Sagheer Ahmed. 2009. "Platelet aggregation, antiglycation, cytotoxic, phytotoxic and antimicrobial activities of extracts of Nepeta juncea." *African Journal of Biotechnology* 8 (6).

Imran, Imran, Liaqat Hussain, Sagheer Ahmad, and Nasir Rasool. 2012. "Antiplatelet activity of methanolic extract of Acacia leucophloea bark." *Journal of Medicinal Plants Research* 6:4185-4188. doi: 10.5897/JMPR12.010.

Institute, National Cancer. 2024. "Cancer Risk and Genetics." https://www.cancer.gov/about-cancer/causes-prevention/genetics.

Israel, Bridg'ette B, Syreeta L Tilghman, Kitani Parker-Lemieux, and Florastina %J Oncology letters Payton-Stewart. 2018. "Phytochemicals: Current strategies for treating breast cancer." 15 (5):7471-7478.

Jiang, Hua, Jingjing Fan, Lin Cheng, Pan Hu, Renbin %J OncoTargets Liu, and therapy.

2018. "The anticancer activity of genistein is increased in estrogen receptor beta 1-positive breast cancer cells."8153-8163.

Johnson, Ian T %J Proceedings of the Nutrition Society. 2007. "Phytochemicals and cancer." 66 (2):207-215.

Kobayashi, Takashi, Teruhiro Nakata, and Takejiro %J Cancer letters Kuzumaki. 2002. "Effect of flavonoids on cell cycle progression in prostate cancer cells." 176 (1):17-23.

Kunnumakkara, Ajaikumar B, Preetha Anand, and Bharat B %J Cancer letters Aggarwal. 2008. "Curcumin inhibits proliferation, invasion, angiogenesis and metastasis of different cancers through interaction with multiple cell signaling proteins." 269 (2):199-225.

Kwong, Ava, Enders KO Ng, Edmund YH Tang, Chris LP Wong, Fian BF Law, Candy PH Leung, Aaron Chan, MT Cheung, MY To, and Edmond SK %J Familial cancer Ma. 2011. "A novel de novo BRCA1 mutation in a Chinese woman with early onset breast cancer." 10:233-237.

Lai, Hung-Wen, Su-Yu Chien, Shou-Jen Kuo, Ling-Ming Tseng, Hui-Yi Lin, Chin-Wen Chi, Dar-Ren %J Evidence-Based Complementary Chen, and Alternative Medicine. 2012. "The potential utility of curcumin in the treatment of HER-2-overexpressed breast cancer: An in vitro and in vivo comparison study with herceptin." 2012 (1):486568.

Lakhani, Sunil R, Jorge S Reis-Filho, Laura Fulford, Frederique Penault-Llorca, Marc van der Vijver, Suzanne Parry, Timothy Bishop, Javier Benitez, Carmen Rivas, and Yves-Jean %J Clinical cancer research Bignon. 2005. "Prediction of BRCA1 status in patients with breast cancer using estrogen receptor and basal phenotype." 11 (14):5175-5180.

Li, Yao, Jiaying Yao, Chunyan Han, Jiaxin Yang, Maria Tabassum Chaudhry, Shengnan Wang, Hongnan Liu, and Yulong %J Nutrients Yin. 2016. "Quercetin, inflammation and immunity." 8 (3):167.

Li, Yuanyuan, Syed M Meeran, Shweta N Patel, Huaping Chen, Tabitha M Hardy, and Trygve O %J Molecular cancer Tollefsbol. 2013. "Epigenetic reactivation of estrogen receptor-α (ERα) by genistein enhances hormonal therapy sensitivity in ERα-negative breast cancer." 12:1-17.

Liu, Ren, Xiaowei Yu, Xin Chen, Hongfei Zhong, Chenglin Liang, Xiaolin Xu, Wenxiu Xu, Yu Cheng, Wei Wang, and Lehan %J Nutrition Research Yu. 2019. "Individual factors define the overall effects of dietary genistein exposure on breast cancer patients." 67:1-16.

Long, Xinghua, Meiyun Fan, Robert M Bigsby, and Kenneth P %J Molecular cancer therapeutics Nephew. 2008. "Apigenin inhibits antiestrogen-resistant breast cancer cell growth through estrogen receptor-α-dependent and estrogen receptor-α-independent mechanisms." 7 (7):2096-2108.

Malone, Kathleen E, Janet R Daling, David R Doody, Li Hsu, Leslie Bernstein, Ralph J Coates, Polly A Marchbanks, Michael S Simon, Jill A McDonald, and Sandra A %J Cancer research Norman. 2006. "Prevalence and predictors of BRCA1 and BRCA2 mutations in a population-based study of breast cancer in white and black American women ages 35 to 64 years." 66 (16):8297-8308.

Martin, S Eric, Mark Sausen, Abraham Joseph, David D Biggs, Brewster F Kingham, Eric S %J Breast cancer research Martin, and treatment. 2009. "BRCA1 E1644X: a deleterious mutation in an African American individual with early onset breast cancer." 113:393-395.

Medicine, U.S. National Library of. 2025. "Genistein and Beast Cancer Clinical Tri-

als." https://clinicaltrials.gov/search?term=genistein&cond=breast%20cancer&viewType=Table.

Mohammad Nabavi, Seyed, Solomon Habtemariam, Maria Daglia, and Seyed %J Anti-Cancer Agents in Medicinal Chemistry Fazel Nabavi. 2015. "Apigenin and breast cancers: from chemistry to medicine." 15 (6):728-735.

Motoyama, Noboru, and Kazuhito Naka. 2004. "DNA damage tumor suppressor genes and genomic instability." *Current opinion in genetics & development* 14 (1):11-16.

Mukund, Vidya %J Current drug metabolism. 2020. "Genistein: its role in breast cancer growth and metastasis." 21 (1):6-10.

Nardin, Simone, Edoardo Mora, Feba Mariam Varughese, Francesca D'Avanzo, Ajay Ram Vachanaram, Valentina Rossi, Chiara Saggia, Sara Rubinelli, and Alessandra %J Frontiers in oncology Gennari. 2020. "Breast cancer survivorship, quality of life, and late toxicities." 10:864.

Narod, Steven A %J Nature reviews Clinical oncology. 2011. "Hormone replacement therapy and the risk of breast cancer." 8 (11):669-676.

Narod, Steven A, and Leonardo Salmena. 2011. "BRCA1 and BRCA2 mutations and breast cancer." *Discovery medicine* 12 (66):445-453.

Organization, World Health. 2023. "Breast Cancer: Key Facts." https://www.who.int/news-room/fact-sheets/detail/breast-cancer.

Organization, World Health. 2024. "Cancer Fact Sheet." https://www.who.int/news-room/fact-sheets/detail/breast-cancer.

Patil, Jeevitha B, Jinhee Kim, and GK %J European journal of pharmacology Jayaprakasha. 2010. "Berberine induces apoptosis in breast cancer cells (MCF-7) through mitochondrial-dependent pathway." 645 (1-3):70-78.

Pilleron, Sophie, Diana Sarfati, Maryska Janssen-Heijnen, Jérôme Vignat, Jacques Ferlay, Freddie Bray, and Isabelle %J International journal of cancer Soerjomataram. 2019. "Global cancer incidence in older adults, 2012 and 2035: a population-based study." 144 (1):49-58.

Prasad, Chandra P, Gayatri Rath, Sandeep Mathur, Dinesh Bhatnagar, and Ranju %J Chemico-biological interactions Ralhan. 2009. "Potent growth suppressive activity of curcumin in human breast cancer cells: Modulation of Wnt/β-catenin signaling." 181 (2):263-271.

Prasad, Chandra P, Gayatri Rath, Sandeep Mathur, Dinesh Bhatnagar, and Ranju %J Chemico-biological interactions Ralhan. 2010. "Expression analysis of maspin in invasive ductal carcinoma of breast and modulation of its expression by curcumin in breast cancer cell lines." 183 (3):455-461.

Pratheeshkumar, Poyil, Amit Budhraja, Young-Ok Son, Xin Wang, Zhuo Zhang, Songze Ding, Lei Wang, Andrew Hitron, Jeong-Chae Lee, and Mei Xu. 2012. "Quercetin inhibits angiogenesis mediated human prostate tumor growth by targeting VEGFR-2 regulated AKT/mTOR/P70S6K signaling pathways."

Priyadarsini, R Vidya, R Senthil Murugan, S Maitreyi, K Ramalingam, D Karunagaran, and S %J European journal of pharmacology Nagini. 2010. "The flavonoid quercetin induces cell cycle arrest and mitochondria-mediated apoptosis in human cervical cancer (HeLa) cells through p53 induction and NF-κB inhibition." 649 (1-3):84-91.

Rahman, Md Mominur, Md Taslim Sarker, Mst Afroza Alam Tumpa, Md Yamin, Tamanna Islam, Moon Nyeo Park, Md Rezaul Islam, Abdur Rauf, Rohit Sharma, and Simona %J Frontiers in Pharmacology Cavalu. 2022. "Exploring the recent trends in perturbing the cellular signaling pathways in cancer by natural products." 13:950109.

Ranganathan, Santhalakshmi, Devaraj Halagowder, and Niranjali Devaraj %J

PloS one Sivasithambaram. 2015. "Quercetin suppresses twist to induce apoptosis in MCF-7 breast cancer cells." 10 (10):e0141370.

Sen, G. S., S. Mohanty, D. M. S. Hossain, S. Bhattacharyya, S. Banerjee, J. Chakraborty, S. Saha, P. Ray, P. Bhattacharjee, D. Mandal, A. Bhattacharya, S. Chattopadhyay, T. Das, and G. Sa. 2011. "Curcumin enhances the efficacy of chemotherapy by tailoring p65NFκB-p300 cross-talk in favor of p53-p300 in breast cancer." *J Biol Chem* 286 (49):42232-42247. doi: 10.1074/jbc.M111.262295.

Sharma, Disha, Sudhanshu Mishra, Aishwarya Rajput, Khushboo Raj, Rishabha %J Current Nutrition Malviya, and Food Science. 2021. "Pathophysiology and biomarkers for breast cancer: Management using herbal medicines." 17 (9):974-984.

Society, American Cancer. 2023. Breast Cancer Facts and Figures 2023.

Song, Qing-Kun, Jing Li, Rong Huang, Jin-Hu Fan, Rong-Shou Zheng, Bao-Ning Zhang, Bin Zhang, Zhong-Hua Tang, Xiao-Ming Xie, and Hong-Jian %J Asian Pacific Journal of Cancer Prevention Yang. 2014. "Age of diagnosis of breast cancer in china: almost 10 years earlier than in the United States and the European union." 15 (22):10021-10025.

Torres-Arzayus, Maria I, Jin Zhao, Roderick Bronson, and Myles Brown. 2010. "Estrogen-dependent and estrogen-independent mechanisms contribute to AIB1-mediated tumor formation." *Cancer research* 70 (10):4102-4111.

Tseng, Tsui-Hwa, Ming-Hsien Chien, Wea-Lung Lin, Yu-Ching Wen, Jyh-Ming Chow, Chi-Kuan Chen, Tsang-Chih Kuo, and Wei-Jiunn %J Environmental toxicology Lee. 2017. "Inhibition of MDA-MB-231 breast cancer cell proliferation and tumor growth by apigenin through induction of G2/M arrest and histone H3 acetylation-mediated p21WAF1/CIP1 expression." 32 (2):434-444.

Walsh, Michael F, Karen Cadoo, Erin E Salo-Mullen, Marianne Dubard-Gault, Zsofia K Stadler, and Kenneth %J Abeloff's clinical oncology Offit. 2020. "Genetic factors: hereditary cancer predisposition syndromes."180-208. e11.

Wang, Liye, Qianyi Lu, Kuikui Jiang, Ruoxi Hong, Shusen Wang, Fei %J Oncology Research Xu, and Treatment. 2022. "BRAF V600E mutation in triple-negative breast cancer: A case report and literature review." 45 (1-2):54-61.

Wu, Anna H, Mimi C Yu, Chui-Chen Tseng, Nathan C Twaddle, and Daniel R %J Carcinogenesis Doerge. 2004. "Plasma isoflavone levels versus self-reported soy isoflavone levels in Asian-American women in Los Angeles County." 25 (1):77-81.

Xie, Qi, Qian Bai, Ling-Yun Zou, Qian-Yong Zhang, Yong Zhou, Hui Chang, Long Yi, Jun-Dong Zhu, Man-Tian %J Genes Mi, Chromosomes, and Cancer. 2014. "Genistein inhibits DNA methylation and increases expression of tumor suppressor genes in human breast cancer cells." 53 (5):422-431.

Xu, Bo, Seong-tae Kim, Michael B %J Molecular Kastan, and cellular biology. 2001. "Involvement of Brca1 in S-phase and G2-phase checkpoints after ionizing irradiation." 21 (10):3445-3450.

Yan, Guang-Rong, Chuan-Le Xiao, Gui-Wei He, Xing-Feng Yin, Nan-Peng Chen, Ya Cao, and Qing-Yu %J Proteomics He. 2010. "Global phosphoproteomic effects of natural tyrosine kinase inhibitor, genistein, on signaling pathways." 10 (5):976-986.

Yang, Jun, Rui Hai %J Journal of agricultural Liu, and food chemistry. 2009. "Synergistic effect of apple extracts and quercetin 3-β-D-glucoside combination on antiproliferative activity in MCF-7 human breast cancer cells in vitro." 57 (18):8581-8586.

Zan, L., Q. Chen, L. Zhang, and X. Li. 2019. "Epigallocatechin gallate (EGCG) suppresses growth and tumorigenicity in breast cancer cells by downregulation of miR-25." *Bioengineered* 10 (1):374-382. doi: 10.1080/21655979.2019.1657327.

Zhao, Qingxia, Ming Zhao, Amanda B Parris, Ying Xing, and Xiaohe %J International Journal of Oncology Yang. 2016. "Genistein targets the cancerous inhibitor of PP2A to induce growth inhibition and apoptosis in breast cancer cells." 49 (3):1203-1210.

Zhou, Q. M., X. F. Wang, X. J. Liu, H. Zhang, Y. Y. Lu, S. Huang, and S. B. Su. 2011. "Curcumin improves MMC-based chemotherapy by simultaneously sensitising cancer cells to MMC and reducing MMC-associated side-effects." *Eur J Cancer* 47 (14):2240-7. doi: 10.1016/j.ejca.2011.04.032.

Zhou, Q. M., H. Zhang, Y. Y. Lu, X. F. Wang, and S. B. Su. 2009. "Curcumin reduced the side effects of mitomycin C by inhibiting GRP58-mediated DNA cross-linking in MCF-7 breast cancer xenografts." *Cancer Sci* 100 (11):2040-5. doi: 10.1111/j.1349-7006.2009.01297.x.

Zhu, W., L. Jia, G. Chen, H. Zhao, X. Sun, X. Meng, X. Zhao, L. Xing, J. Yu, and M. Zheng. 2016. "Epigallocatechin-3-gallate ameliorates radiation-induced acute skin damage in breast cancer patients undergoing adjuvant radiotherapy." *Oncotarget* 7 (30):48607-48613. doi: 10.18632/oncotarget.9495.