Women's health: Harnessing the chemo-preventive potential of phytochemicals for breast cancer


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Abstract
Breast cancer continues to be one of the most prevalent forms of cancer, morbidity and mortality in women globally, with increasing incidence rates projected to surpass 3 million new cases annually by 2040. Current treatment modalities, including surgery, radiation, and chemotherapy, often face limitations such as drug resistance, significant side effects, and poor outcomes for metastatic cases. This highlights the urgent need for effective prevention and treatment strategies. Phytochemicals compounds naturally present in fruits, vegetable and medicinal plants exhibit promising anticancer properties, influencing key biological processes such as cellular proliferation, apoptosis, and metastasis. This review explores the chemo preventive potential of various phytochemicals, including polyphenols, flavonoids, carotenoids, and terpenoids, emphasizing their mechanisms of action and molecular targets relevant to breast cancer. The safety, low toxicity, and accessibility of these compounds position them as viable complementary or alternative options for breast chemoprevention and therapy.

Keywords: Breast cancer, Chemoprevention, Phytochemicals

1. Introduction

Despite significant medical advancements, breast carcinoma remains the second most occurring and lethal cancer impacting women. Over the past four decades, the prevalence of breast cancer has risen dramatically. Around 2.3 million new cases were reported worldwide in 2020, resulting in around 685,000 deaths, with marked geographic differences across various countries and regions. Notably, high-income countries account for a larger share of breast cancer fatalities. Projections indicate that by 2040, there will be over 3 million new cases of breast carcinoma are expected, resulting in more than 1 million mortalities each year (1).

Breast cancer is classified based on the presence of hormone receptors estrogen receptor positive (ER+), progesterone receptor positive (PR+), human epidermal growth factor receptor positive (HER2+), and triple-negative (TNBC), which lacks these receptors. The estrogen receptor (ER) is crucial for diagnosis, as about 70–75% of invasive breast cancers have high ER levels. The progesterone receptor (PR) is found in over 50% of ER-positive patients but is rare in ER-negative cases. PR levels are influenced by ER, indicating a functioning ER pathway. Both ER and PR are commonly found in breast cancer cells and serve as important diagnostic and prognostic markers. HER2 is expressed in about 15–25% of breast cancers (2).

Breast cancer treatments currently include surgical options, radiation therapy, hormone therapy, targeted therapy, immunotherapy, and various chemotherapy drugs such as paclitaxel, doxorubicin, cisplatin, docetaxel, carboplatin, epirubicin, bevacizumab, and cyclophosphamide (3). Nevertheless, these treatments have several limitations, including drug resistance, disease progression, unnecessary exposure of healthy tissues, and a poor prognosis for metastatic breast cancer. Additionally, the significant side effects linked to these therapies have significantly decreased their effectiveness (4,5).

2. Anticancer properties of phytochemicals

An urgent demand exists for developing efficient strategies in the management of breast cancer therapy that has prompted to explore various natural substances as potential supplementary or alternative cancer therapies. Many nature-derived compounds, particularly phytochemicals, have demonstrated anticancer effects by impacting the onset, progression and tumour advancement. They achieve this by regulating numerous mechanisms, such as cell growth, differentiation, programmed cell death, and metastasis. Many cancer treatments currently approved are derived from phytochemicals or their structural analogues, with several of these compounds presently undergoing clinical studies (4,5).

Various phytochemicals have been thoroughly studied for their antitumor properties including examination of safety, minimal toxicity, and wide accessibility contributing to their appeal in cancer research as depicted below (6).

Table 1. Reported phytochemicals in the chemoprevention of breast cancer

S.No.	Phyto-chemicals	Source	Reported anti-cancer activity in breast cancer	Ref
1	Curcumin	*Curcuma longa,* Zingiberaceae (Turmeric)	Curcumin contributes to arrest breast cancer (BC) cells in the cell cycle and notably triggers programmed cell death (apoptosis) in these cells	(7)
2	Resveratrol	*Vitis vinifera,* Vitaceae (Grapes)	The anticancer actions of resveratrol in breast cancer involve the suppression of cell proliferation	(8)
3	Carnosic acid	*Salvia officinalis* L., Lamiaceae (Sage)	Carnosic acid strongly suppresses the development of ER-negative human breast cancer cells	(9)
4	Quercetin	*Punica granatum,* Lythraceae (Promegranate)	The study reported that quercetin can induced G2/M phase arrest in MDA-MB-453 cells lines	(10)
5	Apigenin	*Psidium guajava*, Myrtaceae (Guava)	Apigenin induced programmed cell death; cell cycle halt; suppression of fatty acid synthase (FASN)	(11)
6	Tangeretin	Citrus peels, Rutaceae (Orange)	The antiproliferative effect of Tangerin associated with cell cycle arrest at the G1 phase	(12)

7	Genistein	Glycine max, Fabaceae (Soyabean)	Genistein target the estrogen receptor (ER) human epidermal growth factor receptor-2 (HER2)	(13)
8	Cyanidin	Prunus genus, Rosaceae (Cherries)	Cyanidin inhibit breast cancer cell migration and invasion	(14)
9	Silibinin	*Silybum marianum,* Asteraceae (Milk Thistle)	Silibinin affects both estrogen receptors (ER), α and β; prevents metastasis by inhibiting EMT	(15)
10	Urosilic acid	*Ocimum basilicum,* Lamiaceae (Basil)	Ursolic acid induce G1 cell cycle arrest and promoted mitochondrial-induced programmed cell death in breast cancer cells	(16)
11	Limonene	*Citrus limon,* Rutaceae (Lemon)	Limonin Suppress metastasis in breast cancer via a cyclin D1-dependent pathway	(17)
12	Psoralidin	*Psoralea corylifolia,* Leguminosae (Bemchi)	Psoralidin primarily exerts its anticancer effects by blocking tumor cell growth and triggering apoptosis	(18)
13	Ellagic acid	*Rubus idaeus,* Rosaceae (raspberry)	Ellagic acid Activates of the p53 tumor suppressor pathway; leading to cell cycle arrest	(19)
14	Paclitaxel	*Taxus brevifolia* Taxaceae (Taxol)	Paclitaxel disrupts the dynamics of microtubules and their polymerization, hindering mitosis progression by causing failures in chromosomal segregation, ultimately leading to apoptosis induction and mitotic arrest	(20)

ER-negative: Estrogen receptor negative, EMT: Epithelial–mesenchymal transition, p53: Tumor protein, BC-Breast cancer

3. Future prospects for phytochemical use in breast cancer management

To minimize adverse reactions, there is a potential to combine phytochemicals with approved chemotherapeutic drugs, potentially leveraging nanotechnology approach to improve delivery and reduced toxicity. Encouraging further research into the molecular mechanisms of these compounds, along with initiating clinical trials, is vital to better understand their interactions with current therapies and to validate their efficacy and safety. Additionally, raising public awareness about the cancer-preventive benefits of phytochemicals and educating healthcare professionals on their integration into patient care plans is essential for broader acceptance and application.

4. Conclusion

In conclusion, cancer development is a complex process with multiple influencing factors. The intervention with phytochemicals, whether used alone or in combination, may yield positive effects on cancer chemoprevention. With the identification of several molecular targets for many of these compounds, we can anticipate effective prevention by adopting novel treatment strategies.

References

1. Ye F, Dewanjee S, Li Y, Jha NK, Chen ZS, Kumar A, et al. Advancements in clinical aspects of targeted therapy and immunotherapy in breast cancer. Mol Cancer. 2023 Jul 6;22(1):105.
2. Sinn HP, Kreipe H. A Brief Overview of the WHO Classification of Breast Tumors, 4th Edition, Focusing on Issues and Updates from the 3rd Edition. Breast Care. 2013;8(2):149–54.
3. Younas M, Hano C, Giglioli-Guivarc'h N, Abbasi BH. Mechanistic evaluation of phytochemicals in breast cancer remedy: current understanding and future perspectives. RSC Adv. 2018;8(52):29714–44.
4. Amin ARMR, Kucuk O, Khuri FR, Shin DM. Perspectives for Cancer Prevention with Natural Compounds. Journal of Clinical Oncology. 2009 Jun 1;27(16):2712–25.
5. Chen D, Dou QP. Tea Polyphenols and Their Roles in Cancer Prevention and Chemotherapy. Int J Mol Sci. 2008 Jul 12;9(7):1196–206.
6. Inami K, Mine Y, Tatsuzaki J, Mori C, Mochizuki M. Isolation and characterization of antimutagenic components of Glycyrrhiza aspera against N-methyl-N-nitrosourea. Genes and Environment. 2017 Dec 6;39(1):5.
7. Zhu J, Li Q, Wu Z, Xu Y, Jiang R. Curcumin for Treating Breast Cancer: A Review of Molecular Mechanisms, Combinations with Anticancer Drugs, and Nanosystems. Pharmaceutics. 2024 Jan 5;16(1):79.
8. Behroozaghdam M, Dehghani M, Zabolian A, Kamali D, Javanshir S, Hasani Sadi F, et al. Resveratrol in breast cancer treatment: from cellular effects to molecular mechanisms of action. Cellular and Molecular Life Sciences. 2022 Nov 4;79(11):539.
9. Birtić S, Dussort P, Pierre FX, Bily AC, Roller M. Carnosic acid. Phytochemistry. 2015 Jul;115:9–19.
10. Tang SM, Deng XT, Zhou J, Li QP, Ge XX, Miao L. Pharmacological basis and new insights of quercetin action in respect to its anti-cancer effects. Biomedicine & Pharmacotherapy. 2020 Jan;121:109604.
11. Adel M, Zahmatkeshan M, Akbarzadeh A, Rabiee N, Ahmadi S, Keyhanvar P, et al. Chemotherapeutic effects of Apigenin in breast cancer: Preclinical evidence and molecular mechanisms; enhanced bioavailability by nanoparticles. Biotechnology Reports. 2022 Jun;34:e00730.
12. Surichan S, Arroo RR, Tsatsakis AM, Androutsopoulos VP. Tangeretin inhibits the proliferation of human breast cancer cells via CYP1A1/CYP1B1 enzyme induction and CYP1A1/CYP1B1–mediated metabolism to the product 4′ hydroxy tangeretin. Toxicology in Vitro. 2018 Aug;50:274–84.
13. Konstantinou EK, Gioxari A, Dimitriou M, Panoutsopoulos GI, Panagiotopoulos AA. Molecular Pathways of Genistein Activity in Breast Cancer Cells. Int J Mol Sci. 2024 May 20;25(10):5556.
14. Chen D, Yuan M, Ye Q, Wang X, Xu J, Shi G, et al. Cyanidin-3-O-glucoside inhibits epithelial-to-mesenchymal transition, and migration and invasion of breast cancer cells by upregulating KLF4. Food Nutr Res. 2020 Sep 28;64(0).
15. Binienda A, Ziolkowska S, Pluciennik E. The Anticancer Properties of Silibinin: Its Molecular Mechanism and Therapeutic Effect in Breast Cancer. Anticancer Agents Med Chem. 2020 Oct 27;20(15):1787–96.
16. Yin R, Li T, Tian JX, Xi P, Liu RH. Ursolic acid, a potential anticancer compound for breast cancer therapy. Crit Rev Food Sci Nutr. 2018 Mar 4;58(4):568–74.
17. Miller JA, Lang JE, Ley M, Nagle R, Hsu CH, Thompson PA, et al. Human Breast Tissue Disposition and Bioactivity of Limonene in Women with Early-Stage Breast Cancer. Cancer Prevention Research. 2013 Jun 1;6(6):577–84.
18. Meng D, Dong Y, Shang Q, Sun Z. Anti-tumor effect and hepatotoxicity mechanisms of psoralen. Front Pharmacol. 2024 Aug 5;15.
19. Golmohammadi M, Zamanian MY, Jalal SM, Noraldeen SAM, Ramírez-Coronel AA, Oudaha KH, et al. A comprehensive review on Ellagic acid in breast cancer treatment: From cellular effects to molecular mechanisms of action. Food Sci Nutr. 2023 Dec 18;11(12):7458–68.
20. Abu Samaan TM, Samec M, Liskova A, Kubatka P, Büsselberg D. Paclitaxel's Mechanistic and Clinical Effects on Breast Cancer. Biomolecules. 2019 Nov 27;9(12):789.
21. Sohel M, Aktar S, Biswas P, Amin Md Al, Hossain MdA, Ahmed N, et al. Exploring the anti-cancer potential of dietary phytochemicals for the patients with breast cancer: A comprehensive review. Cancer Med. 2023 Jul 3;12(13):14556–83.