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Research progress of natural products in prevention and treatment of breast cancer

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Abstract:

Breast cancer, as a highly prevalent cancer, receives significant attention. Natural products have numerous advantages in the treatment of breast cancer. Natural products, such as plant extracts and marine organism extracts, may contain various compounds with potential anticancer activity. Natural products have shown promising anti-tumor activity, paving the way for the exploration of novel anticancer agents. Many natural products have demonstrated certain anticancer activity in laboratory and animal models, influencing processes such as proliferation, apoptosis, invasion, and metastasis of cancer cells. These studies provide preliminary evidence for further research. This article summarizes some commonly used natural products and their roles in breast cancer.

Keywords: Brest cancer, Natural products, Traditional Chinese medicine, Plants

1. Introduction

Breast cancer manifests as a malignant tumor originating from the epithelial cells of the breast tissue, constituting one of the foremost malignancies afflicting women worldwide. Among the various cancer types observed in 2020, breast cancer exhibited the highest incidence rate, making up 11.7% of all reported cases. Subsequently, lung cancer (11.4%), colorectal cancer (10.0%), prostate cancer (7.3%), and stomach cancer (5.6%) ranked among the top in terms of prevalence.[1] The specific causes of breast cancer are currently not fully understood, but they are believed to be associated with factors such as gender, age, hormones, and others. Breast cancer typically originates from the lobules or ducts of the breast, and as cancer cells grow and divide abnormally, a tumor forms. Through the mechanism of hematogenous or lymphatic spread, these malignant cells can travel to remote areas of the body, prompting the occurrence of distant metastatic disease. Surgical excision of the tumor, radiation therapy, chemotherapy, hormone therapy, and targeted therapy are among the treatment modalities available for breast cancer. The selection and customization of the treatment approach depend on factors such as cancer type, stage, and individual considerations. Traditional treatment methods often come with significant side effects, including digestive issues such as loss of appetite, diarrhea, or constipation; immune system reactions such as immunosuppression and increased risk of infection; hair loss due to certain chemotherapy drugs; skin changes such as dryness, rashes, or pigmentation; and blood-related problems such as anemia, decreased platelets, or decreased white blood cells. Natural products have been widely studied for their potential in breast cancer treatment due to their minimal side effects, low toxicity, and efficacy based on multitargeted therapy. They have demonstrated anticancer activity against breast cancer by inhibiting angiogenesis, cell migration, proliferation, and tumor growth. This article summarizes several common natural products that have shown potential in the treatment of breast cancer.

2. NATIONAL COMPOUNDS

2.1 .*Soybean*

Soybean is a legume plant and an important staple and oilseed crop. It originated in East Asia and is one of the most important crops worldwide. Soybean is a high-protein, low-fat plant food that is rich in quality proteins, dietary fiber, vitamins, and minerals. Among its components, soybean also contains soy isoflavones, which are believed to have certain benefits for the treatment and prevention of breast cancer. Soy isoflavones are a type of plant compound belonging to the flavonoid class. In soybeans, the main isoflavones include genistein, daidzein, and glycitein. These compounds can be metabolized into active compounds, such as equol and intestinal bacterial metabolites, in the body. [2] Soy isoflavones possess phytoestrogenic activity and can bind to estrogen receptors,

influencing the levels of endogenous estrogen and modulating estrogen signaling. This may have an impact on the treatment and prevention of estrogen-dependent breast cancer.[3]

2.2 *Euphorbia*

Euphorbia is a type of succulent plant that belongs to the family Euphorbiaceae. The Euphorbiaceae family is a large plant family that includes many species and varieties, with Euphorbia being one of the most well-known and widely distributed genera. The latex extract of Euphorbia is a milky substance obtained from the stems and leaves of the plant. Euphorbia latex is a complex mixture containing various components, some of which are active compounds. Traditional medicine has used Euphorbia latex for the treatment of skin warts and certain benign tumors. Its toxic constituents may exert irritative and destructive effects on diseased tissues. The latex extract obtained from Euphorbia bicolor, along with its bioactive compounds, demonstrates remarkable inhibitory properties against ER-positive breast cancer cell lines (MCF-7 and T47-D) and triple-negative breast cancer cell lines (MDA-MB-231 and MDA-MB-468), while exhibiting no inhibitory effects on human normal primary dermal fibroblasts.[4] Isolated from the latex of Euphorbia resinifera, a compound structurally resembling the ingol skeleton, specifically 7-p-methoxyphenylacetate-3,8,12-triacetate, demonstrates cytotoxic properties against the MCF7 breast cancer cell line.[5] Continued scientific exploration into the molecular mechanisms through which latex phytochemicals operate in ER-positive and triple-negative breast cancer cell lines holds promise for the discovery and development of potential therapeutic modalities for breast cancer.

2.3 *Saffron*

Saffron is a precious spice and medicinal plant that plays an important role in cooking, medicine, and cultural traditions. Its unique flavor, aroma, and color make it an indispensable ingredient in numerous cuisines and food preparations. The chemical analysis of Ukrainian saffron (Crocus sativus stigmas) has identified the presence of seven compounds, namely crocetin, picrocrocin, safranal, rutin, apigenin, caffeic acid, and ferulic acid. Significantly, crocetin, picrocrocin, safranal, rutin, and apigenin emerge as the key active components in Ukrainian saffron. Ethanol extract exhibited a significant decrease in viability of MDA-MB-231 and IGR39 cells compared to water extract, and it showed stronger effects. Purified apigenin and caffeic acid compounds demonstrated significant cytotoxic effects on breast cancer, melanoma, and glioblastoma cell lines, suggesting their promising role as cytotoxic agents against these cancers.[6] Identifying resveratrol as one of the compounds present in Crocus sativus leaf revealed its ability to inhibit proliferation in human breast cancer MDA-MB-453 cells, as well as the mouse melanoma cell line B16F1 and human malignant melanoma cell line A375.[7]

2.4 *Bitter melon*

The vegetable and medicinal plant Momordica charantia, commonly called bitter melon, is widely distributed in tropical and subtropical regions. Bitter melon is rich in various nutrients, including vitamin C, vitamin A, vitamin K, dietary fiber, and antioxidants. Additionally, it contains minerals such as potassium, magnesium, iron, and zinc. Despite its bitter taste, bitter melon is considered to have medicinal value. It possesses natural antibacterial and antiparasitic properties. It is used in traditional medicine to treat certain infections and parasitic diseases. By triggering mitochondrial damage via the generation of reactive oxygen species (ROS), the extract obtained from bitter melon vesicles exerted a robust apoptotic-inducing effect on 4T1 cells. The CCK-8 assay results indicate that bitter melon-derived vesicles extract can inhibit the proliferation of 4T1 and MCF-7 cells, with visible effects observed after 12 hours of treatment. As a prospective natural nanomedicine, the extract derived from vesicles of bitter melon demonstrates robust anti-tumor effects on breast cancer cells, both in cellular studies and animal models, with no notable adverse effects.[8, 9] To summarize, bitter melon holds promise as a natural medicinal option that can be used alone or in combination with conventional radiation and chemotherapy to aid in the prevention and treatment of breast cancer, ovarian cancer, and cervical cancer.

2.5 *Reishi mushroom*

Recognized as Lingzhi or Reishi, Ganoderma lucidum is a popular herb and edible mushroom that is widely recognized. It is a woody, saprophytic fungus belonging to the Ganodermataceae family. Lingzhi has a long history and extensive use in traditional Chinese medicine and herbal remedies. Abundant in diverse antioxidant compounds like polyphenols and flavonoids, it aids in neutralizing free radicals, alleviating oxidative stress, and displaying anti-inflammatory characteristics. Consequently, Lingzhi has the potential to be beneficial in averting inflammation and the emergence of chronic diseases. The triterpenoid compounds found in Lingzhi, known as meroterpenoid dimers, have long been regarded as the primary active components with anti-tumor properties. Rac exhibits abnormal activity in various cancers and is associated with tumor invasion and metastasis. Overactivated Rac can promote cancer cell migration, increase tumor infiltration, and contribute to metastasis. Therefore, Rac is considered

a potential target for cancer treatment and metastasis inhibition. By inhibiting Rac activity, Ganoderma lucidum extract demonstrates the capacity to suppress cancer cell migration and invasion. In a dose-dependent manner, Ganoderma lucidum extract decreases the viability of the MDA-MB-231 triple-negative breast cancer cell line, which is characterized by its high invasiveness and aggressive nature.[10] The Ganoderma lucidum methanolic extract demonstrates significant toxicity against MCF-7 and K-562 cancer cells.[11]

2.6 *Houttuynia cordata*

Houttuynia cordata Thunb, commonly known as Fish Mint or Fish Herb, is primarily found in Asian regions such as China, Japan, Korea, and Southeast Asia. It thrives in moist environments and is often found growing near rivers, lakes, swamps, and wetlands. Houttuynia cordata is widely used in traditional herbal medicine. Its leaves, stems, and roots contain volatile oils, flavonoids, flavonols, tannins, and various nutrients. In traditional Chinese medicine, Houttuynia cordata is believed to have properties such as heat-clearing, detoxification, anti-inflammatory, diuretic, antibacterial, and antiviral effects. It is commonly used to treat conditions such as colds, coughs, gastroenteritis, eczema, and rheumatism. The cell cytotoxicity of both Houttuynia cordata extract and its individual components was examined on MDA-MB-231 and MCF-7 human breast cancer cells, as well as NIH3T3 normal mouse fibroblast cells. Cell apoptosis and oxidative stress, induced by the production of hydrogen peroxide and superoxide anion free radicals, played a crucial role in the potent growth-inhibitory effects of a specific extract and dosage of Houttuynia cordata on human invasive breast cancer cells. The Houttuynia cordata thunb extract downregulates the expression of cell cycle proteins D1 and CDK4, thereby inhibiting colony formation and inducing G1 cell cycle arrest in MCF-7 and MDA-MB-231 cells. In addition, the Houttuynia cordata thunb extract exerts its apoptotic effects in MCF-7 and MDA-MB-231 cells through a caspase-dependent pathway.[12, 13] In conclusion, these findings provide a theoretical basis for further investigating the potential effects of Houttuynia cordata thunb extract on breast cancer in vivo.

2.7 *Green tea*

Green tea is a variety of tea that experiences minimal oxidation and processing, ensuring that the tea leaves retain their natural color and vibrant green appearance. Green tea contains various components such as caffeine, catechins, amino acids, chlorophyll, and vitamin C. Among them, catechins are one of the most important constituents in green tea. They belong to a class of antioxidants and include epicatechin, epicatechin gallate, catechin gallate, and catechin tetramer, among others. By significantly diminishing the accumulation of myeloid-derived suppressor cells and augmenting the CD4+ to CD8+ T cell ratio, the green tea polyphenol EGCG effectively improves immune suppression in 4T1 breast tumor mice, particularly in the spleen and tumor microenvironment.[14] Matcha green tea extract decreases the cell viability of T47D cells, resulting in the overexpression of PPARγ at the protein and mRNA levels.[15] Green tea, as a natural food, has not only been consumed as part of a healthy diet but also shows potential as an anticancer agent. Large-scale clinical studies are still underway to further understand the role of green tea in cancer prevention and treatment.

3. CONCLUSIONS

Many natural products have shown anticancer effects in vitro and animal experiments, providing preliminary evidence for further preclinical research to evaluate their efficacy and mechanisms in cancer prevention and treatment. Natural products often contain multiple active components that may act on cancer through multiple pathways. This multi-modality may help overcome drug resistance of cancer cells and enhance treatment efficacy. Natural products generally have fewer toxic side effects compared to conventional therapies. However, despite being generally considered relatively safe, certain natural products may have adverse effects and toxicity. Therefore, toxicity assessment and safety studies of natural products are crucial. While potential anticancer activity has been demonstrated in the laboratory and animal models, there is currently a lack of sufficient evidence for the clinical efficacy of many natural products in human cancer treatment. Most natural products have not yet undergone clinical trials, and therefore, their efficacy and safety require further research and validation. In conclusion, the use of natural products in cancer treatment is a promising field, but more research is needed to validate their efficacy and safety.

REFERENCES

1. Sung, H.; Ferlay, J.; Siegel, R. L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F., Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 2021, *71* (3), 209-249.

2. Yue, Z.; He, S.; Wang, J.; Jiang, Q.; Wang, H.; Wu, J.; Li, C.; Wang, Z.; He, X.; Jia, N., Glyceollins from soybean: Their pharmacological effects and biosynthetic pathways. *Heliyon* 2023, *9* (11), e21874.

3. Chen, L. R.; Chen, K. H., Utilization of Isoflavones in Soybeans for Women with Menopausal Syndrome: An Overview.

Int J Mol Sci 2021, *22* (6).
4. Basu, P.; Meza, E.; Bergel, M.; Maier, C., Estrogenic, Antiestrogenic and Antiproliferative Activities of Euphorbia bicolor (Euphorbiaceae) Latex Extracts and Its Phytochemicals. *Nutrients* 2019, *12* (1).
5. Ourhzif, E. M.; Ricelli, A.; Stagni, V.; Cirigliano, A.; Rinaldi, T.; Bouissane, L.; Saso, L.; Chalard, P.; Troin, Y.; Khouili, M.; Akssira, M., Antifungal and Cytotoxic Activity of Diterpenes and Bisnorsesquiterpenoides from the Latex of Euphorbia resinifera Berg. *Molecules* 2022, *27* (16).
6. Mykhailenko, O.; Petrikaite, V.; Korinek, M.; El-Shazly, M.; Chen, B. H.; Yen, C. H.; Hsieh, C. F.; Bezruk, I.; Dabrisiute, A.; Ivanauskas, L.; Georgiyants, V.; Hwang, T. L., Bio-guided bioactive profiling and HPLC-DAD fingerprinting of Ukrainian saffron (Crocus sativus stigmas): moving from correlation toward causation. *BMC Complement Med Ther* 2021, *21* (1), 203.
7. Mykhailenko, O.; Petrikaite, V.; Korinek, M.; Chang, F. R.; El-Shazly, M.; Yen, C. H.; Bezruk, I.; Chen, B. H.; Hsieh, C. F.; Lytkin, D.; Ivanauskas, L.; Georgiyants, V.; Hwang, T. L., Pharmacological Potential and Chemical Composition of Crocus sativus Leaf Extracts. *Molecules* 2021, *27* (1).
8. Feng, T.; Wan, Y.; Dai, B.; Liu, Y., Anticancer Activity of Bitter Melon-Derived Vesicles Extract against Breast Cancer. *Cells* 2023, *12* (6).
9. Psilopatis, I.; Vrettou, K.; Giaginis, C.; Theocharis, S., The Role of Bitter Melon in Breast and Gynecological Cancer Prevention and Therapy. *International Journal of Molecular Sciences* 2023, *24* (10).
10.Acevedo-Diaz, A.; Ortiz-Soto, G.; Suarez-Arroyo, I. J.; Zayas-Santiago, A.; Martinez Montemayor, M. M., Ganoderma lucidum Extract Reduces the Motility of Breast Cancer Cells Mediated by the RAC(-)Lamellipodin Axis. *Nutrients* 2019, *11* (5).
11.Mousavi, S. M.; Hashemi, S. A.; Gholami, A.; Omidifar, N.; Chiang, W. H.; Neralla, V. R.; Yousefi, K.; Shokripour, M., Ganoderma lucidum methanolic extract as a potent phytoconstituent: characterization, in-vitro antimicrobial and cytotoxic activity. *Sci Rep* 2023, *13* (1), 17326.
12.Subhawa, S.; Chewonarin, T.; Banjerdpongchai, R., The Effects of Houttuynia cordata Thunb and Piper ribesioides Wall Extracts on Breast Carcinoma Cell Proliferation, Migration, Invasion and Apoptosis. *Molecules* 2020, *25* (5).
13.Inthi, P.; Pandith, H.; Kongtawelert, P.; Banjerdpongchai, R., Anti-cancer Effect and Active Phytochemicals of Houttuynia cordata Thunb. against Human Breast Cancer Cells. *Asian Pac J Cancer Prev* 2023, *24* (4), 1265-1274.
14.Xu, P.; Yan, F.; Zhao, Y.; Chen, X.; Sun, S.; Wang, Y.; Ying, L., Green Tea Polyphenol EGCG Attenuates MDSCs-mediated Immunosuppression through Canonical and Non-Canonical Pathways in a 4T1 Murine Breast Cancer Model. *Nutrients* 2020, *12* (4).
15.Keckstein, S.; Tilgener, C.; Jeschke, U.; Hofmann, S.; Vilsmaier, T.; Kaltofen, T.; Heidegger, H.; Batz, F.; Mahner, S.; Schroder, L., Effects of matcha tea extract on cell viability and peroxisome proliferator-activated receptor gamma expression on T47D breast cancer cells. *Arch Gynecol Obstet* 2022, *306* (2), 451-459.