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**Original Research Article**

# A Review on Phytochemical Compounds Used to Treatment of Breast Cancer

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**Abstract:** Breast cancer remains one of the leading causes of cancer-related mortality among women worldwide. Recent research has highlighted the potential of phytochemicals, bioactive compounds derived from plants, in the prevention and treatment of various cancers, including breast cancer. This study reviews the therapeutic effects of specific phytochemicals-curcumin, resveratrol, quercetin, sulforaphane, and genistein-focusing on their anti-cancer properties, mechanisms of action, and potential applications. Using a systematic literature review, key studies involving in vitro, in vivo, and clinical research were analyzed to evaluate each compound's efficacy in inhibiting tumor growth, inducing apoptosis, and preventing metastasis. The findings suggest that these phytochemicals may offer significant benefits in breast cancer treatment through multiple mechanisms, including anti-inflammatory and antioxidant activities, hormone modulation, and inhibition of cancer cell proliferation. However, further research, particularly large-scale clinical trials, is needed to optimize formulation strategies and validate their efficacy in clinical settings.

**Keywords:** Breast Cancer, phytochemical compounds, used to treatment.



## 01. INTRODUCTION

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells in the body. These cells can form tumors or spread through the blood and lymphatic systems to other parts of the body in a process called metastasis. Cancer can develop in almost any organ or tissue, such as the lungs, breast, colon, prostate, and skin.

There are many types of cancer, classified based on the type of cell or organ from which they originate. For example, carcinomas arise from the skin or the tissues lining internal organs, sarcomas come from connective tissues like bone or muscle, while leukemia originates in the blood-forming tissues.

The causes of cancer are complex and include genetic factors, environmental exposures (such as tobacco smoke, radiation, and certain chemicals), infections, and lifestyle choices (like diet and physical activity). The symptoms of cancer vary depending on the type and stage of the disease but may include unexplained weight loss, fatigue, pain, changes in skin appearance, or abnormal lumps.

Cancer treatment often involves surgery, radiation therapy, chemotherapy, immunotherapy, or targeted therapy, depending on the type and stage of the disease. Early detection and advancements in medical research have led to better outcomes for many cancer patients.

However, cancer remains a leading cause of death worldwide.

**02. Objective of the Study**

Purpose of the study the purpose of a study on breast cancer can vary depending on the research question, but generally, breast cancer studies aim to:

1. Understand the Causes: Investigate genetic, environmental, and lifestyle factors that contribute to the development of breast cancer.
2. Improve Early Detection: Develop or refine screening methods, such as mammography or blood tests, to identify breast cancer at earlier, more treatable stages.
3. Treatment Advancement: Test new treatments, therapies, or drugs to improve survival rates, reduce side effects, and prevent recurrence. This could include chemotherapy, targeted therapies, or immunotherapies.
4. Survival and Prognosis: Investigate factors that affect survival rates, including tumor biology, response to treatment, and patient characteristics.
5. Quality of Life: Assess how treatment affects the physical and emotional well-being of individuals diagnosed with breast cancer.
6. Prevention: Explore strategies to prevent breast cancer, such as lifestyle changes or genetic interventions for high-risk individuals.

**03. Breast Cancer:**

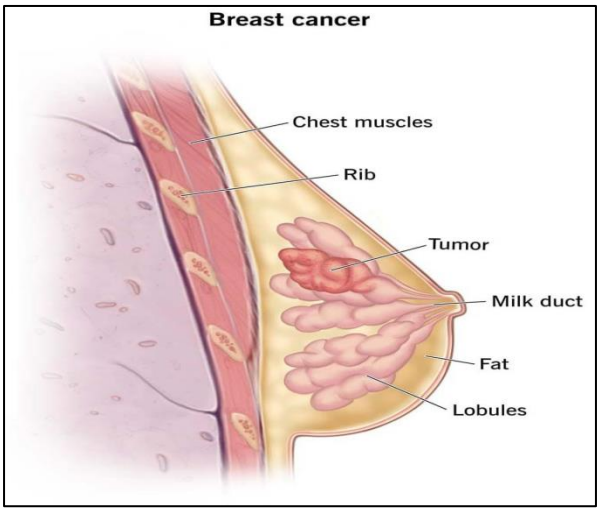


**Figure-01: Breast Cancer**

Breast cancer is a type of cancer that begins in the cells of the breast. It can develop in both men and women, though it is far more common in women. The disease occurs when abnormal cells in the breast grow uncontrollably, forming a tumor that can spread to nearby tissues or other parts of the body.

**04. Type of Breast Cancer:**

There are many types of breast cancer, which are invasive and non -invasive.

**1. Invasive Breast Cancer:**

These cancers have spread beyond the ducts or lobules into surrounding breast tissue.

- Invasive Ductal Carcinoma (IDC): The most common type of breast cancer, starting in the milk ducts and then spreading to surrounding tissue.
- Invasive Lobular Carcinoma (ILC): Begins in the milk-producing glands (lobules) and then spreads. This type can be harder to detect on mammograms.
- Inflammatory Breast Cancer (IBC): A rare but aggressive form where the breast becomes red, swollen, and warm. It can cause the skin to appear dimpled or pitted.
- Medullary Carcinoma: A rare form of IDC, it typically has a better prognosis than other invasive types and is characterized by distinct, soft, and well-defined tumor boundaries.
- Mucinous (Colloid) Carcinoma: A less common type, where the cancer cells produce mucus and form well-defined tumor boundaries.

**2. Non-invasive (In Situ) Breast Cancer These are early-stage cancers where abnormal cells are present but have not spread beyond their point of origin.**

- Ductal Carcinoma in Situ (DCIS): Abnormal cells are found in the milk ducts but have not invaded surrounding tissues. It's considered a pre-cancerous condition.
- Lobular Carcinoma in Situ (LCIS): Abnormal cells are found in the milk-producing lobules,

but it's not considered true cancer. However, it indicates a higher risk of developing invasive breast cancer later.

**3. Other Subtypes**

Triple-Negative Breast Cancer: A type of IDC that lacks estrogen, progesterone, and HER2 receptors. It tends to be more aggressive and has fewer treatment options.

- HER2-Positive Breast Cancer: Characterized by excess HER2 protein on the cancer cells, this type tends to grow and spread more quickly, but targeted therapies like Herceptin can be effective.
- Hormone Receptor-Positive (ER/PR Positive): These cancers test positive for estrogen and/or progesterone receptors, meaning they grow in response to hormones. They are more likely to respond to hormone therapy.
- Paget's Disease of the Nipple: A rare type of cancer that starts in the milk ducts and spreads to the skin of the nipple and areola.

**4. Rare Types of Breast Cancer**

1. **Phyllodes Tumor:** A rare tumor that develops in the connective tissue of the breast. It can be benign or malignant.
2. **Angiosarcoma:** A rare cancer originating in the blood vessels of the breast.

**05. Biological Activity:**

The biological activity of cancer refers to the processes by which cancer cells grow, spread, and evade normal biological controls. Unlike normal cells, cancer cells exhibit uncontrolled division and survival, which are driven by various genetic mutations and environmental factors. Key aspects of cancer's biological activity include:

1. **Uncontrolled Cell Proliferation:** Cancer cells bypass normal growth signals and often continue dividing even in the absence of external growth factors. This is often due to mutations in genes that regulate cell cycle progression (e.g., mutations in proto-oncogenes like Ras or tumor suppressor genes like p53).
2. **Evading Apoptosis:** Cancer cells develop mechanisms to resist programmed cell death (apoptosis), which allows them to survive when they would normally be eliminated. This can occur through mutations in genes like Bcl-2 or defects in the p53 pathway.
3. **Angiogenesis:** Tumors can stimulate the growth of new blood vessels (angiogenesis) to supply themselves with nutrients and oxygen. This is often mediated by the secretion of factors like vascular endothelial growth factor (VEGF).
4. **Invasion and Metastasis:** Cancer cells acquire the ability to invade surrounding tissues and spread to distant organs. This involves changes in cell adhesion molecules (e.g., E-cadherin) and the production of enzymes (e.g., matrix metalloproteinases) that degrade extracellular matrices.
5. **Genomic Instability:** Cancer cells typically display an increased rate of mutations, chromosomal abnormalities, and loss of genomic integrity. This contributes to tumor heterogeneity and can provide a selective advantage for cancer progression.
6. **Immune Evasion:** Cancer cells can develop ways to evade the immune system, including by expressing immune checkpoint proteins like PD-L1, which suppress immune cell activity, or by recruiting immune-suppressive cells into the tumor microenvironment.
7. **Metabolic Reprogramming:** Cancer cells often undergo metabolic changes, such as the Warburg effect, where they favor glycolysis over oxidative phosphorylation, even in the presence of oxygen. This helps meet the demands of rapid growth and survival.

## 06. METHODOLOGY

This review was conducted through a systematic analysis of published literature on phytochemicals with potential therapeutic effects against breast cancer. Key databases, including Google Scholar, PubMed, and Scopus, were utilized to identify relevant studies. Search terms such as "breast cancer," "phytochemicals," "Curcumin," "Resveratrol," "Quercetin," "Sulforaphane," "Epigallocatechin gallate," and "Genistein" were used to locate articles on each compound's biological activity, therapeutic effects, and mechanisms of action against breast cancer cells.

The selected studies included both in vitro and in vivo research that examined the efficacy, mechanisms, and safety of these phytochemicals. Inclusion criteria focused on studies that provided detailed analyses of the compounds' molecular pathways, effects on breast cancer cell lines, or impact on tumor progression in animal models.

Each compound's bioactivity was analyzed based on reported effects such as antioxidant properties, anti-inflammatory actions, apoptosis induction, angiogenesis inhibition, and interaction with cancer cell signaling pathways. Comparative analysis was performed to synthesize information across studies, identifying common therapeutic pathways and evaluating their potential for integrative cancer treatment.

This methodology aimed to consolidate findings from multiple studies, providing a comprehensive overview of phytochemical

compounds' roles in breast cancer treatment while highlighting areas requiring further clinical research.

**07. Literature Review:**

The literature review was conducted using reputable databases such as Google Scholar, PubMed, and Scopus. Search terms included combinations of keywords like "breast cancer," "phytochemicals," "curcumin," "resveratrol," "quercetin," "sulforaphane," "genistein," and "anti-cancer activity." Filters were applied to retrieve studies published in English within the last 10 years to ensure relevance and up-to-date findings.

**08. Phytochemical Analysis:**

Phytochemicals are bioactive compounds naturally occurring in plants, which have been extensively studied for their health benefits, particularly in cancer prevention and therapy. The efficacy of these compounds in breast cancer is linked to their ability to interfere with cancer cell signaling pathways, induce apoptosis, inhibit metastasis, and improve oxidative stress response. This section analyzes specific phytochemicals known for their anticancer activity and therapeutic potential in breast cancer treatment.

**09. Curcumin:**

Curcumin is the active compound found in turmeric, a spice derived from the root of the Curcuma longa plant. It has been studied for its wide range of potential health benefits due to its anti-inflammatory, antioxidant, and anticancer properties.

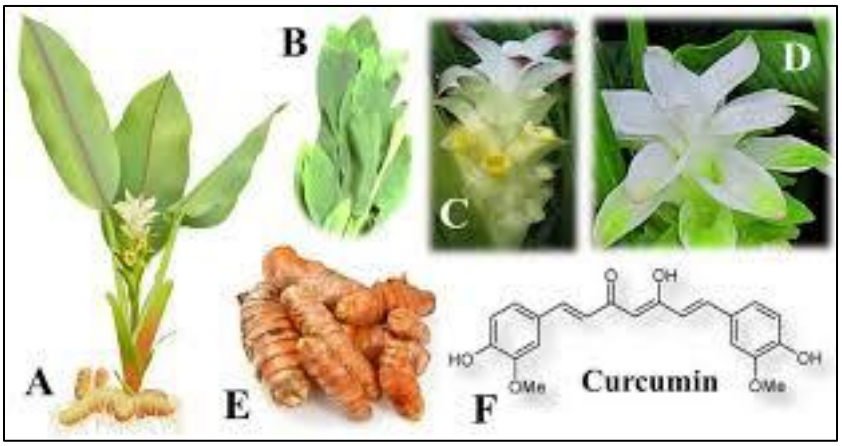


**Figure-02: structure of curcumin**

**09.1. Source:**

Curcumin is primarily sourced from the rhizomes (underground stems) of the turmeric plant, Curcuma longa, which belongs to the ginger family. Turmeric rhizomes are dried and ground into a powder, with curcumin making up about 2-8% of this turmeric powder. This powdered turmeric is then commonly used as a spice, dietary supplement, and natural dye.

**09.2. Mechanism of Action:**

Carcumin.
↓
Curcumin block cancer cell proliferation such as NF-kB, PI3/AKT, MAPK.
↓
Curcumin activate the Apoptosis.
↓
Inhibit angiogenesis
↓
Inhibition the formation of blood vessels.

**09.3. Use:**

Curcumin is used in various ways, due to potential health benefit:

®. Anti-inflammatory and pain relief.
®. Antioxidants.
®. Digestive systems.
®. Cancer prevention.
®. Dietary supplement.
®. Skin care.

**10. Resveratrol:**

Resveratrol, a non flavonoids polyphenol. Resveratrol is part of a group of compounds called polyphenols. They're thought to act like antioxidants, protecting the body against damage that can put you at higher risk for things like cancer and heart disease.

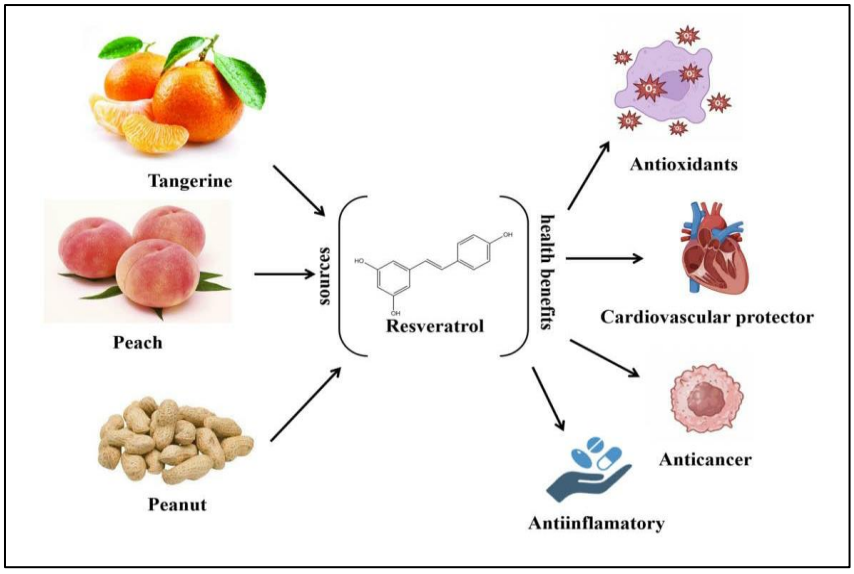


**Figure-03: structure of Resveratrol**

**10.1. Source:**

®. Red wine.
®. Berries.
®. Penuts.
®. Red graps.

**10.2. Mechanism of Action:**

Resveratrol acts on several molecular targets, including the estrogen receptor, p53, and various pro-inflammatory cytokines.

↓

It inhibits aromatase, an enzyme essential for estrogen synthesis, which is particularly relevant in hormone-dependent breast cancers.

↓

Resveratrol also enhances the efficacy of other therapies by sensitizing cancer cells to chemotherapy and radiotherapy.

**10.3. Use:**

®. Anti- inflammatory.
®. Cancer prevention.
®. Heart disease.

**11. Quercetin:**

Quercetin is a plant-derived flavonoid, a type of antioxidant compound found in various fruits, vegetables, and grains. It is known for its potential health benefits, including reducing inflammation, acting as an antihistamine, and protecting cells from oxidative stress. Quercetin is often used in supplements for its purported effects on boosting immune function, improving cardiovascular health, and alleviating allergy symptoms.

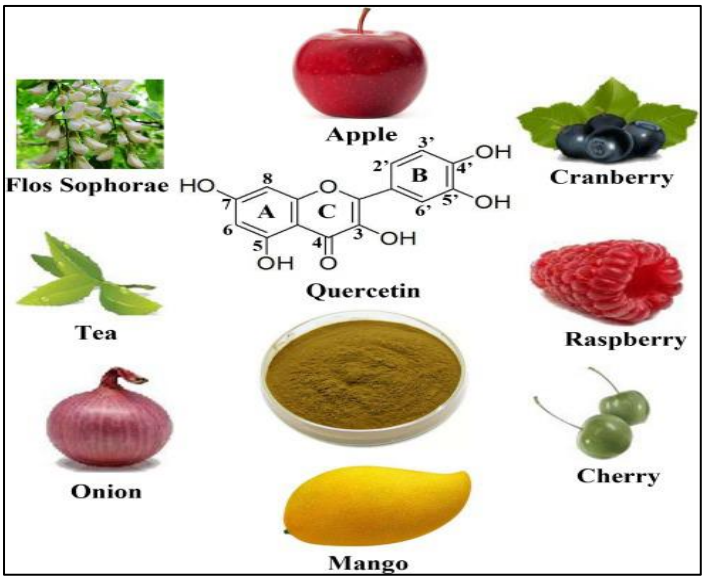


**Figure-04: Structure of Quercetin**

**11.1. Source:**

1. Onions (especially red onions).
2. Apples.
3. Berries (such as blueberries, blackberries, and cranberries)
4. Citrus fruits (oranges, grapefruits).
5. Grapes.
6. Cherries.
7. Leafy greens (like spinach and kale).
8. Broccoli.
9. Cabbage.
10. Green tea.

**11.2. Mechanism of Action:**

Quercetin exhibits anticancer properties by modulating MAPK/ERK and PI3K/AKT pathways.

↓

It induces apoptosis, inhibits angiogenesis, and reduces oxidative stress within cancer cells. Quercetin also interacts with inflammatory mediators, lowering the inflammatory response, which is often heightened in cancer.

**11.3. Use:**

®. Reduce swelling.
®. Kill cancer cells.
®. Diabetes.
®. Control blood pressure.
®. Arthritis.

**12. Sulforaphane:**

Sulforaphane is a powerful antioxidant compound primarily found in cruciferous vegetables.

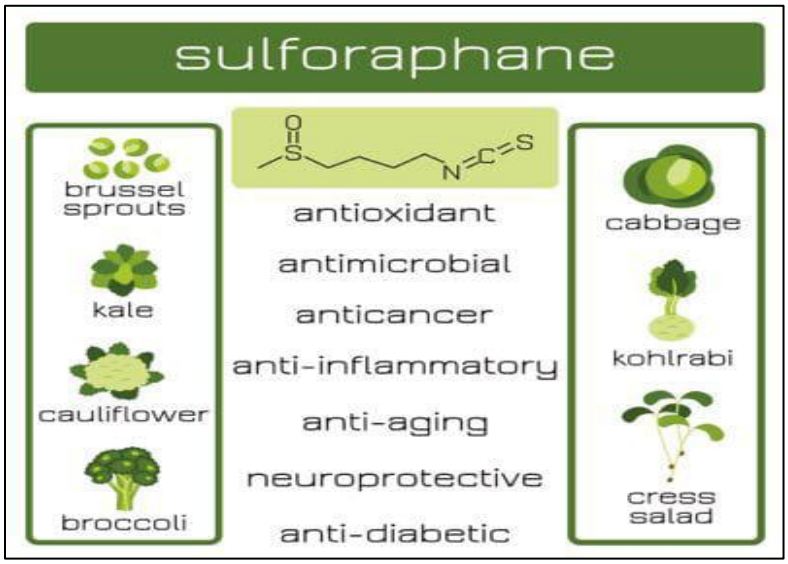


**Figure-05: structure of sulforaphane.**

**12.1. Source:**

®. Broccoli sprouts.
®. Broccoli
®. kale.
®. Cauliflower.
®. Cabbage.

**12.2. Mechanism of Action:**

Sulforaphane activates Nrf2, a transcription factor involved in the cellular response to oxidative stress, and inhibits histone deacetylase (HDAC), which plays a role in cancer cell proliferation.

↓

It also targets cancer stem cells, which are often resistant to conventional treatments and implicated in metastasis.

**12.3. Use:**

As a powerful antioxidant, sulforaphane supports overall health and has potential as a chemopreventive agent. In breast cancer therapy, it may help prevent recurrence by targeting cancer stem cells and reducing tumor growth.

**13. Epiglallocatechin Gallate:**

Epiglallocatechin-3-gallate (EGCA) is the major polyphonolic constituent found in green tea leaves of the camellia sinensis.

Epiglallocatechin gallate also known as Epiglallocatechin -3 gallate is the ester of Epiglallocatechin and gallic acid and is a type of catchin.

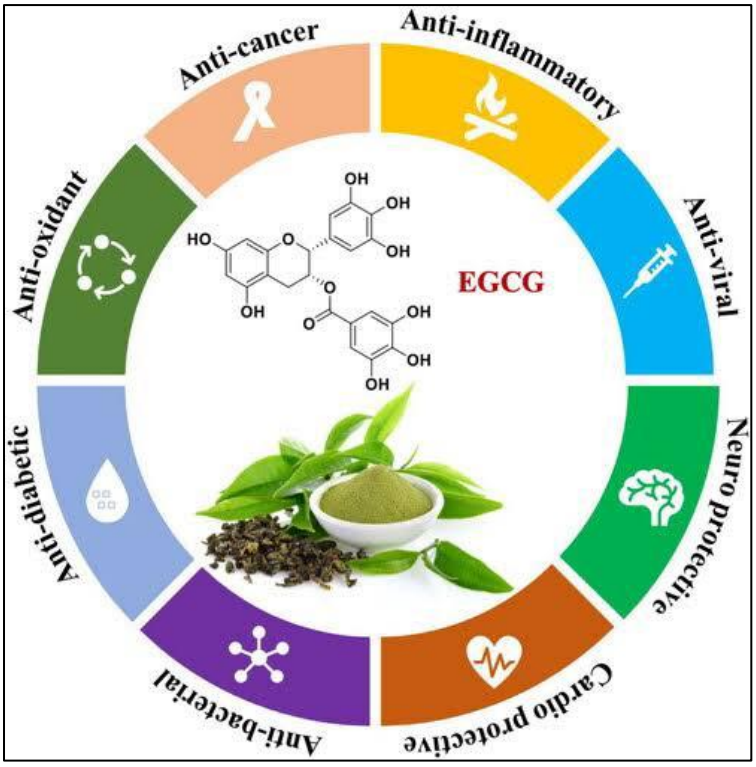


**Figure-06: structure of Epiglallocatechin gallate.**

**13.1. Source:**

®. Green tea.

®. others tea.

**13.2. Mechanism of Action:**

EGCG inhibits the growth of breast cancer cells by downregulating signaling pathways such as STAT3, VEGF, and EGFR, which are involved in tumor growth, angiogenesis, and metastasis.

↓

It also induces apoptosis by modulating the expression of Bcl-2 family proteins.

**13.3. Use:**

EGCG is often consumed in the form of green tea or as a dietary supplement. Its chemopreventive properties make it useful in reducing breast cancer risk and as a complementary treatment to reduce tumor progression.

**14.Genistein:**

Genistein is a naturally occurring compounds that structurally belongs to a class of compounds known as isoflavons. It is described as an angiogenesis inhibitor and phytoestrogen.

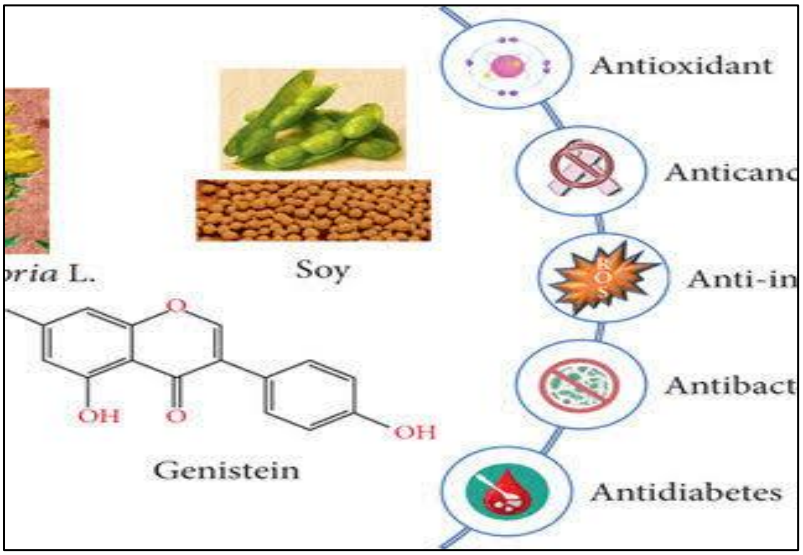


**Figure-07: structure of Genistein**

**14.1. Source:**

®. Tofu.

®. Soybean.

**14.2. Mechanism of Action:**

Genistein acts as both an estrogen agonist and antagonist, making it particularly relevant in hormone-dependent breast cancer.

↓

It inhibits breast cancer cell proliferation and invasion and modulates the PI3K/AKT and MAPK pathways.

↓

Additionally, genistein has anti-angiogenic properties, which reduce blood supply to tumors, thus inhibiting growth.

**14.3. Use:**

Genistein is commonly used as a dietary supplement, particularly in regions with high soy consumption. In breast cancer, it is valued for its ability to inhibit cancer cell growth and improve the efficacy of hormone therapies.

**15. In Vivo and In Vitro Studies:**

Both in vitro (cell culture) and in vivo (animal) studies are essential for understanding the mechanisms and therapeutic potential of phytochemicals in treating breast cancer. In vitro studies help researchers explore the direct effects of phytochemicals on cancer cells in a controlled lab setting, while in vivo studies examine these effects within living organisms, providing insight into bioavailability, metabolism, and systemic responses.

**In Vitro Studies:**

In vitro studies involve testing phytochemicals on cultured breast cancer cells to analyze their effects on cell proliferation, survival, and gene expression. The following are common in vitro methods used in studying phytochemicals:

1. Breast Cancer Cell Lines: Cell lines such as MCF-7, T47D, and MDA-MB-231 are frequently used, each representing different subtypes of breast cancer (e.g., hormone receptor-positive or triple-negative). These cell lines provide a platform for screening phytochemicals for cytotoxicity and anti-cancer effects.
2. Cell Viability and Proliferation Assays: Compounds are tested for their ability to inhibit cancer cell growth through assays like MTT, which measures cell viability, and colony formation assays, which assess the compound's effect on cell proliferation.
3. Apoptosis and Cell Cycle Analysis: Phytochemicals are evaluated for their capacity to induce apoptosis (programmed cell death) and arrest the cell cycle. Flow cytometry and Western blotting are used to detect markers of apoptosis, such as cleaved caspase-3, and proteins involved in cell cycle regulation.
4. Mechanistic Studies: In vitro research allows detailed analysis of how phytochemicals affect cancer cells at the molecular level, targeting pathways related to inflammation, oxidative stress, and angiogenesis. Techniques include PCR for gene expression analysis and Western blotting for protein expression.
5. 3D Cell Cultures: To better mimic the tumor microenvironment, 3D cell cultures, such as spheroids or organoids, are sometimes employed. These models provide a more realistic view of tumor responses to phytochemicals compared to 2D cultures.

**In Vivo Studies:**

In vivo studies involve testing the effects of phytochemicals in animal models, often mice or rats, to observe their therapeutic potential in a living organism. These studies help determine the compound's bioavailability, toxicity, and overall effect on tumor growth and metastasis in a biological context.

1. Animal Models of Breast Cancer: Common models include xenografts, where human breast cancer cells are implanted in immunocompromised mice, and genetically engineered mouse models that spontaneously develop breast tumors. These models allow for evaluation of phytochemicals' therapeutic efficacy in reducing tumor size and spread.
2. Dosage and Administration: Phytochemicals are administered to animals in various forms, such as oral supplementation, intraperitoneal injection, or topical application. Studies vary the dosages to determine optimal therapeutic levels and examine dose-dependent effects.
3. Tumor Growth Inhibition: Tumor volume and weight are measured to assess the impact of phytochemicals on breast cancer progression. Compounds are evaluated for their ability to reduce tumor size and slow metastasis.
4. Biomarker Analysis: Blood samples and tissue sections from treated animals are analyzed to monitor biomarkers of apoptosis, angiogenesis, and immune response. Techniques like immunohistochemistry and ELISA are used to measure changes in protein and cytokine levels in response to treatment.
5. Toxicity and Side Effects: In vivo studies assess potential side effects by monitoring

weight changes, organ toxicity, and blood markers for liver and kidney function. This is essential for determining the safety profile of phytochemicals before clinical trials in humans.

**Comparative Result from In Vitro and In Vivo Studies:**

®. Consistency in Findings: Many phytochemicals, such as curcumin, resveratrol, and genistein, have shown consistent results in both in vitro and in vivo studies, particularly in inducing apoptosis and reducing tumor growth.

®. Limitations of In Vitro Findings: While in vitro studies are valuable for initial screening, they may not fully capture the compound's effectiveness in an organism, as factors like metabolism and bioavailability differ in a living system.

## 16. CONCLUSION

The findings of this review underscore the promising role of phytochemicals in the treatment of breast cancer. Compounds like curcumin, resveratrol, quercetin, sulforaphane, and genistein have demonstrated significant anti-cancer activities, including tumor inhibition, apoptosis induction, and metastasis prevention. These phytochemicals offer a natural, less toxic alternative or complement to traditional cancer treatments, potentially improving patient outcomes and quality of life. However, while preclinical studies provide compelling evidence, more comprehensive clinical trials are essential to confirm their therapeutic potential and safety. Future research should focus on optimizing the delivery and bioavailability of these compounds and exploring combination therapies to enhance their efficacy.

This review contributes to the growing evidence supporting phytochemicals as valuable resources in the fight against breast cancer, offering new avenues for personalized and targeted treatment options.

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