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Research Article

A Comprehensive Review of Anticancer Phytochemicals: Mechanisms, Efficacy and Therapeutic Potential

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ABSTRACT

Breast cancer remains one of the leading causes of cancer-related morbidity and mortality among women worldwide. Although current treatment strategies—such as chemotherapy, radiotherapy, endocrine therapy, and targeted molecular therapies—have significantly improved survival outcomes, they are often limited by adverse effects, resistance development, and high treatment costs. These limitations have increased interest in identifying safer, more accessible, and multi-targeted therapeutic options. Dietary phytochemicals, naturally occurring bioactive compounds present in fruits, vegetables, grains, herbs, and medicinal plants, have gained considerable attention for their anticancer potential. A growing body of evidence shows that these compounds can modulate several hallmarks of cancer, including uncontrolled cell proliferation, metastasis, inflammation, angiogenesis, oxidative stress, and dysregulated signaling pathways. Phytochemicals exert their actions through multiple molecular targets such as PI3K/Akt/mTOR, NF-κB, MAPK, Wnt/β-catenin, STAT3, Nrf2, caspases, and microRNAs, thereby suppressing tumor development at various stages. This review provides an organized and comprehensive overview of key dietary phytochemicals, their natural sources, and their mechanistic roles in breast cancer prevention and therapy. By summarizing current experimental and mechanistic evidence, this article highlights their therapeutic promise and emphasizes the need for continued research and clinical validation.

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer and one of the major causes of cancer-related death among women. The global burden of this disease continues to rise, influenced by genetic, hormonal, environmental, and lifestyle factors. While advancements in early detection and therapeutic interventions have improved

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prognosis, treatment challenges persist, particularly in aggressive subtypes such as triple-negative breast cancer (TNBC).

Current therapies—including surgery, radiation, chemotherapy, immunotherapy, endocrine therapy, and targeted agents—can be effective, but many patients experience severe side effects, reduced quality of life, and, in some cases, treatment failure due to drug resistance. These limitations underscore the importance of exploring alternative or complementary therapeutic approaches that are safer, more affordable, and capable of targeting multiple cancer-related pathways.

Dietary phytochemicals have emerged as promising candidates in this regard. These naturally occurring plant compounds are abundant in commonly consumed foods such as vegetables, fruits, legumes, nuts, spices, and medicinal herbs. Phytochemicals such as curcumin, genistein, quercetin, epigallocatechin gallate (EGCG), resveratrol, lycopene, and sulforaphane have been extensively studied for their antioxidant, anti-inflammatory, and anticancer activities. Remarkably, nearly 70% of existing anticancer agents are derived from natural sources, demonstrating the substantial therapeutic potential of plant-based compounds.

A key advantage of phytochemicals is their ability to act on multiple cellular and molecular targets simultaneously. They can regulate essential processes including cell-cycle progression, programmed cell death, angiogenesis, metastasis, oxidative stress, and immune responses. Moreover, they can modulate epigenetic mechanisms and influence the expression of tumour-suppressive or oncogenic microRNAs, expanding their functional significance.

Despite extensive experimental research, the collective understanding of how dietary phytochemicals influence breast cancer pathways requires consolidation. Therefore, this review aims to present a clearer, reorganized, and mechanistically focused understanding of the anticancer roles of major dietary phytochemicals, with emphasis on their signalling targets, therapeutic significance, and current gaps in clinical translation.

2. SOURCES AND CLASSIFICATION OF DIETARY PHYTOCHEMICALS :

Dietary phytochemicals are naturally occurring; non-nutritive bioactive compounds present in a wide variety of plant-based foods. Although they are not essential nutrients like vitamins or minerals, they play critical roles in maintaining cellular health and protecting the body against various diseases, including cancer. Their abundance in commonly consumed fruits, vegetables, spices, grains, legumes, and medicinal herbs makes them an easily accessible and cost-effective source of natural therapeutic agents.

Phytochemicals are highly diverse in structure and biological activity, but they can be broadly classified into several major groups based on their chemical composition. These include **polyphenols, terpenoids, alkaloids, organosulfur compounds, and carotenoids**. Each group contains multiple compounds with distinct mechanisms of action that collectively contribute to their anticancer potential.

2.1 Polyphenols

Polyphenols are among the most extensively studied phytochemicals and include flavonoids, phenolic acids, lignans, and stilbenes. They are widely distributed in fruits, vegetables, tea, wine, nuts, and seeds.

Common Examples & Sources:

- **Flavonoids:** quercetin (onions, apples, leafy greens), kaempferol (broccoli, spinach), epigallocatechin gallate (green tea), luteolin (celery, carrots).
- **Phenolic acids:** caffeic acid (coffee, berries), ferulic acid (whole grains), Rosmarinus acid (herbs like rosemary and basil).
- **Stilbenes:** resveratrol (grapes, berries, peanuts).
- **Isoflavones:** genistein and daidzein (soybeans, tofu, legumes).

Relevance to Breast Cancer:

Polyphenols exhibit potent antioxidant, anti-inflammatory, and anti-proliferative effects. Many have structural similarities to estrogenic and can modulate estrogenic receptor (ER) activity, making them relevant to hormone-dependent breast cancers.

2.2 Terpenoids and Triterpenes

Terpenoids are found in aromatic plants, spices, and medicinal herbs. They include a broad group of compounds such as monoterpenes, diterpenes, and triterpenoids.

Common Examples & Sources:

- **Curcumin** (turmeric)
- **Limonene** (citrus peel)
- **Boswellia acids** (*Boswellia serrata*)
- **Withaferin A** (*With Ania somnifera*, ashwagandha)
- **Ginsenosides** (ginseng)
- **Ursolic acid** (apple peel, rosemary, holy basil)

Relevance:

Terpenoids are known for their ability to regulate inflammation, induce apoptosis, and modulate various signalling pathways involved in tumour growth and metastasis.

2.3 Carotenoids

Carotenoids are pigmented compounds responsible for the red, orange, and yellow colours of many fruits and vegetables.

Common Examples & Sources:

- **Lycopene** (tomatoes, watermelon, papaya)
- **β-carotene** (carrots, sweet potatoes)
- **Lutein & Zeaxanthin** (spinach, kale, corn)

Relevance:

Carotenoids possess strong antioxidant properties and can reduce oxidative stress—a key factor in cancer development. Lycopene has shown significant anti-proliferative effects in breast cancer models.

2.4 Organosulfur Compounds

These compounds are derived mainly from Allium (garlic, onion) and Brassica (broccoli, cabbage) vegetables.

Common Examples & Sources:

- **Allicin, Diallyl disulfide (DADS)** — garlic
- **Sulforaphane** — broccoli, kale, cabbage
- **Indole-3-carbinol (I3C)** — cruciferous vegetables

Relevance:

Organosulfur compounds help modulate carcinogen metabolism, detoxification enzymes, oxidative stress, and epigenetic modifications.

2.5 Alkaloids

Alkaloids are nitrogen-containing compounds with diverse biological activities.

Common Examples & Sources:

- **Piperine** (black pepper)
- **Berberine** (barberry, turmeric)
- **Calprotectin derivatives** (from *Camptotheca acuminata*)

Relevance:

Many alkaloids are used clinically as chemotherapeutic agents. Berberine, for instance, exhibits strong anti-proliferative activity in breast cancer cells through pathway regulation.

2.6 Other Notable Phytochemical Groups

Some compounds do not fall neatly into the above categories but still demonstrate strong anticancer potential:

- **Ellagitannins:** pomegranate
- **Saponins:** legumes, soy
- **Phenylpropanoids:** ginger, cloves
- **Xanthones:** mangosteen
- **Lignans:** flax seeds, sesame

3. MECHANISTIC INSIGHTS: HOW DIETARY PHYTOCHEMICALS COUNTERACT BREAST CANCER

Dietary phytochemicals exert anticancer effects through multiple interconnected mechanisms that influence the initiation, progression, and metastasis of breast tumours. Unlike conventional chemotherapeutic drugs—typically designed to target a single molecule or pathway—phytochemicals offer a broader, multitargeted therapeutic profile. This characteristic is especially valuable in breast cancer, a disease known for its molecular complexity and heterogeneous subtypes.

The following subsections summarize the key mechanisms through which phytochemicals modulate cancer cell behaviour and interfere with tumour development.

3.1 Inhibition of Uncontrolled Cell Proliferation

Uncontrolled cell division is a central hallmark of cancer. Many phytochemicals act by suppressing signalling pathways and proteins that promote excessive proliferation, while enhancing pathways that maintain normal cell-cycle regulation.

- **Downregulation of cyclins and cyclin-dependent kinases (CDKs)** Compounds such as curcumin, sesame, and Rosmarinus acid decrease expression of cyclin D1 and CDK4, slowing the transition from G1 to S phase.
- **Activation of tumour suppressor proteins** Silibinin and genistein enhance p53 and p21 levels, leading to controlled cell-cycle arrest.
- **Suppression of growth factor signalling** Formononetin inhibits the FGFR2–Akt

cascade, reducing mitogenic signalling and angiogenesis.

- **Regulation of PI3K/Akt and MAPK pathways**
  These pathways are frequently hyperactivated in breast cancer. Phytochemicals such as curcumin, quercetin, and genistein are known inhibitors.

Representative Examples:

- **Curcumin** reduces NF-κB activity and suppresses cyclin D1, CDK4, and MMP1.
- **Genistein** blocks IGF-1R/PI3K/Akt signalling and enhances pro-apoptotic proteins.
- **Lycopene** increases Bax expression and decreases proliferative markers.
- **Sesame** reduces cyclin D1 and impairs G1/S progression.

Overall, these actions collectively hinder tumour expansion and sensitize cancer cells to therapeutic interventions.

3.2 Induction of Apoptosis (Programmed Cell Death)

Apoptosis is a controlled form of cell death that removes damaged or malignant cells. Many cancer cells evade apoptosis, leading to unchecked growth. Phytochemicals can restore apoptotic pathways by targeting intrinsic (mitochondrial) and extrinsic (death receptor) mechanisms.

- **Modulation of Bcl-2 family proteins**
  Compounds such as curcumin, berberine, and resveratrol decrease anti-apoptotic proteins (Bcl-2, Bcl-xl) and increase pro-apoptotic proteins (Bax, Bak).
- **Activation of caspases**
  Silibinin, ginsenosides, and withaferin A activate caspase-3, -7, -8, and -9, initiating apoptotic cascades.
- **Mitochondrial membrane depolarization**
  Lycopene, EGCG, and sulforaphane promote cytochrome c release, triggering caspase-dependent apoptosis.
- **Regulation of p53 signalling**
  Many phytochemicals restore p53 function, enabling DNA damage recognition and apoptosis.

Representative Examples:

- **Curcumin** triggers mitochondrial apoptosis through caspase-3 and Bax upregulation.
- **Resveratrol** promotes ROS production and enhances death receptor signalling.
- **Withaferin A** disrupts cytoskeletal proteins and activates intrinsic apoptotic pathways.
- **Berberine** increases p53 and decreases Bcl-2, leading to apoptosis in ER^+ and triple-negative breast cancer cells.

Together, these mechanisms help remove malignant cells and prevent tumour persistence.

3.3 Suppression of Metastasis and Invasion

Metastasis is responsible for most of the breast cancer–related deaths. Phytochemicals prevent the spread of cancer cells by interfering with processes such as epithelial–mesenchymal transition (EMT), cell migration, and extracellular matrix degradation.

- **Inhibition of EMT markers**
  Compounds like curcumin and resveratrol

reduce N-cadherin, vimentin, and Snail while upregulating E-cadherin.

- **Downregulation of matrix metalloproteinases (MMPs)**
  MMP-2 and MMP-9 enable invasion; quercetin, EGCG, and luteolin suppress their activity.

- **Blockage of pro-metastatic signalling (NF-κB, STAT3, Wnt/β-catenin)**
  Many phytochemicals inhibit these pathways, reducing cell migration and adhesion.

- **Regulation of chemokines and adhesion molecules**
  Terpenoids such as withaferin A alter integrins and cytokines that support metastasis.

Representative Examples:

- **Resveratrol** inhibits NF-κB and Wnt/β-catenin, preventing cell migration.

- **EGCG** suppresses MMPs and reduces migratory potential.

- **Curcumin** downregulates vimentin and reduces invasive capacity in TNBC cells.

These mechanisms reduce the likelihood of secondary tumour formation.

3.4 Anti-Angiogenic Effects

Tumours require a blood supply to grow and metastasize. Phytochemicals can limit tumour angiogenesis by inhibiting vascular endothelial growth factor (VEGF) and other angiogenic mediators.

Key Mechanisms:

- **Inhibition of VEGF/VEGFR signalling**
  Curcumin, resveratrol, and genistein suppress VEGF expression.

- **Downregulation of hypoxia-inducible factor (HIF-1α)**
  Lycopene and sulforaphane reduce HIF-1α stabilization in hypoxic tumour environments.

- **Suppression of angiogenic cytokines**
  EGCG and quercetin reduce IL-6, TNF-α, and COX-2–dependent angiogenesis.

Representative Examples:

- **Genistein** decreases VEGF production in ER^+ breast cancer models.

- **Resveratrol** blocks HIF-1α accumulation under hypoxia.

- **Curcumin** inhibits angiogenic signalling through NF-κB and Akt.

3.5 Anti-Inflammatory and Antioxidant Actions

Chronic inflammation and oxidative stress are major contributors to breast cancer development. Many phytochemicals exhibit strong anti-inflammatory and antioxidant properties.

- **Downregulation of NF-κB and pro-inflammatory cytokines**
  Curcumin, EGCG, and filicinin inhibit IL-6, TNF-α, COX-2, and ins.

- **Activation of Nrf2 antioxidant pathway**
  Sulforaphane and resveratrol stimulate Nrf2, enhancing cellular antioxidant defences.

- **Reduction of reactive oxygen species (ROS)**
  Carotenoids, quercetin, and phenolic acids decrease ROS levels and prevent DNA damage.

This mechanism helps maintain cellular integrity and reduces mutation risk.

3.6 Epigenetic Modulation

Epigenetic changes play a crucial role in cancer progression. Phytochemicals can modify epigenetic marks that regulate gene expression.

- **Modulation of DNA methylation** EGCG and genistein inhibit DNA methyltransferases (DNMTs).
- **Regulation of histone acetylation** Curcumin and resveratrol can inhibit HDACs and promote tumour-suppressor gene expression.
- **Influence on microRNAs** Many phytochemicals upregulate tumour-suppressor miRNAs and downregulate oncogenic miRNAs.

This epigenetic plasticity contributes to their multi-targeted anticancer actions.

3.7 Immunomodulatory Effects

Some phytochemicals enhance immune surveillance and support antitumor immune responses.

Key Mechanisms:

- Activation of cytotoxic T cells and NK cells
- Suppression of immunosuppressive cytokines
- Modulation of macrophage polarization

Terpenoids, flavonoids, and carotenoids have all shown immunomodulatory potential in breast cancer models.

4. DIETARY PHYTOCHEMICALS AND THEIR SPECIFIC EFFECTS IN BREAST CANCER

Breast cancer encompasses several subtypes with distinct molecular features, and phytochemicals have shown the ability to target a wide spectrum of these variations. This section summarizes the most extensively investigated dietary phytochemicals, their natural sources, and their mechanistic actions against breast cancer.

4.1 Curcumin

Source: *Curcuma longa* (turmeric)
Chemical Class: Polyphenolic curcuminoid

Curcumin is one of the most widely studied natural compounds due to its broad pharmacological profile. In breast cancer, its anticancer activity is attributed to its ability to regulate multiple cellular pathways simultaneously.

Major Mechanisms:

- Inhibits NF-κB, STAT3, and PI3K/Akt signalling
- Reduces expression of cyclin D1, CDK4, and MMPs
- Induces mitochondrial apoptosis through Bax upregulation
- Suppresses angiogenesis by downregulating VEGF
- Inhibits EMT by reducing vimentin and Snail

Curcumin is especially beneficial in **triple-negative breast cancer (TNBC)** models where conventional therapies are limited.

4.2 Resveratrol

Source: Grapes, berries, peanuts
Chemical Class: Stilbene

Resveratrol acts as a potent antioxidant and inhibitor of several oncogenic pathways.

Mechanisms of Action:

- Inhibits Wnt/β-catenin and NF-κB pathways
- Activates p53-mediated apoptosis
- Decreases MMP activity, limiting invasion
- Suppresses HIF-1α and VEGF expression under hypoxia
- Enhances ROS production in cancer cells leading to apoptosis

Resveratrol is known for its multi-targeted action, demonstrating strong anti-proliferative and anti-metastatic potential.

4.3 Genistein

Source: Soybeans and soy-based foods
Chemical Class: Isoflavone (phytoestrogen)

Genistein has structural similarity to estrogenic, enabling it to interact with estrogenic receptors.

Mechanisms of Action:

- Modulates ERα and ERβ activity in hormone-dependent breast cancer
- Inhibits IGF-1R/PI3K/Akt signalling
- Enhances p21 and p53 levels
- Induces apoptosis via mitochondrial pathways
- Reduces angiogenesis by suppressing VEGF

Genistein is particularly relevant for ER-positive breast cancer due to its hormonal interactions.

4.4 Epigallocatechin-3-Gallate (EGCG)

Source: Green tea
Chemical Class: Catechin (polyphenol)

EGCG is the major bioactive compound in green tea with potent anticancer effects.

Mechanisms of Action:

- Suppresses PI3K/Akt and MAPK pathways
- Inhibits MMP-2 and MMP-9, reducing metastasis
- Reduces COX-2 and pro-inflammatory cytokines
- Induces apoptosis via modulation of Bcl-2 family proteins
- Blocks angiogenesis through VEGF inhibition

EGCG's anti-metastatic effects make it a valuable candidate for preventing cancer progression.

4.5 Lycopene

Source: Tomatoes, watermelon, papaya
Chemical Class: Carotenoid

Lycopene is a powerful antioxidant known for reducing oxidative stress and regulating tumour growth.

Mechanisms of Action:

- Enhances Bax expression and reduces Bcl-2, promoting apoptosis
- Suppresses IGF-1–mediated proliferation
- Reduces HIF-1α–dependent angiogenesis

- Scavenges reactive oxygen species (ROS)

Lycopene's antioxidant capacity plays a major role in preventing DNA damage and reducing carcinogenesis.

4.6 Berberine

Source: Barberry, turmeric, *Berberi's* species **Chemical Class:** Is quinoline alkaloid

Berberine has shown significant antiproliferative and pro-apoptotic activity across various breast cancer models.

Mechanisms of Action:

- Downregulates Bcl-2 and activates caspase-3
- Induces p53-dependent apoptosis
- Inhibits AMPK/mTOR signalling
- Reduces invasion by suppressing MMPs

Berberine also enhances the effects of chemotherapeutic drugs, making it a promising adjuvant.

4.7 Withaferin A

Source: *With Ania somnifera* (Ashwagandha) **Chemical Class:** Steroidal lactone (tamanolide)

Withaferin A exhibits strong anti-inflammatory, anti-metastatic, and pro-apoptotic effects.

Mechanisms of Action:

- Disrupts cytoskeletal proteins, inducing apoptosis
- Inhibits NF-κB and STAT3 signalling
- Suppresses EMT by restoring E-cadherin expression
- Decreases tumour invasiveness by inhibiting vimentin

It is particularly effective in aggressive breast cancer subtypes.

4.8 Sulforaphane

Source: Broccoli, cabbage, Brussels sprouts **Chemical Class:** Isothiocyanate

Known for its chemo preventive potency, sulforaphane acts through detoxification pathways.

Mechanisms of Action:

- Activates Nrf2 antioxidant pathway
- Inhibits HDACs, promoting expression of tumour suppressor genes
- Induces G2/M cell-cycle arrest
- Triggers apoptosis in ER-positive and TNBC cells
- Reduces breast cancer stem cell population

Its dual role in detoxification and epigenetic modulation makes it unique.

4.9 Quercetin

Source: Onions, apples, leafy greens **Chemical Class:** Flavanol (polyphenol)

Quercetin shows broad-spectrum anticancer activity.

Mechanisms of Action:

- Inhibits PI3K/Akt and NF-κB signalling
- Reduces COX-2 and TNF-α levels

- Blocks invasion by decreasing MMP-2/9
- Induces apoptosis via mitochondrial pathways

Quercetin's anti-inflammatory and anti-metastatic actions contribute to its therapeutic relevance.

4.10 Other Notable Phytochemicals

- **Apigenin:** suppresses angiogenesis and induces apoptosis
- **Kaempferol:** inhibits PI3K/Akt signalling and EMT
- **Imboiled:** induces ROS-mediated apoptosis (from neem)
- **Rosmarinus acid:** decreases COX-2 and inhibits proliferation
- **Ginsenosides:** modulate immune responses and suppress metastasis
- **Sesamin:** reduces cyclin D1 and inhibits cell cycle progression

Each of these compounds contributes to a broader framework of phytochemical-based breast cancer prevention and therapy.

5. DISCUSSION: CLINICAL RELEVANCE, CHALLENGES, AND FUTURE PERSPECTIVES

Dietary phytochemicals have gained significant attention as complementary or alternative therapeutic agents for breast cancer due to their wide availability, favourable safety profile, and ability to target multiple molecular pathways simultaneously. The evidence accumulated from in vitro studies, animal models, and limited clinical trials demonstrates that many phytochemicals possess strong antiproliferative, pro-apoptotic, anti-metastatic, and anti-inflammatory activities. Despite these promising findings, the translation of phytochemicals into mainstream cancer therapy remains challenging. This section discusses the major strengths, limitations, and future directions for integrating phytochemicals into breast cancer management.

5.1 Clinical Relevance and Therapeutic Advantages

1. Multi-Targeted Mechanisms

Unlike conventional chemotherapeutic agents that primarily target a single molecule or pathway, phytochemicals often interact with multiple cellular targets. This is highly beneficial for breast cancer, a disease driven by complex and interconnected signalling pathways such as PI3K/Akt, MAPK, NF-κB, and STAT3.

2. Low Toxicity and Better Tolerability

Most phytochemicals exhibit minimal toxicity toward normal cells, making them ideal candidates for long-term use or combination with standard therapies.

3. Potential for Chemoprevention

Many phytochemicals act as antioxidants, anti-inflammatory agents, or modulators of hormone activity, making them suitable for preventing cancer in high-risk populations.

4. Enhancement of Chemotherapy and Radiotherapy

Certain phytochemicals, including curcumin, genistein, EGCG, and resveratrol, have shown synergistic effects with chemotherapy by:

- Sensitizing Cancer Cells to Drugs
- Reducing Multi-Drug Resistance

- Protecting Normal Tissues from Treatment-Induced Toxicity
- Enhancing Apoptosis

5. Influence on Cancer Stem Cells

Compounds such as sulforaphane, curcumin, and resveratrol reduce the self-renewal capacity of breast cancer stem cells, potentially minimizing relapse and metastasis.

Collectively, these advantages support the therapeutic relevance of phytochemicals in integrative cancer care.

5.2 Challenges and Limitations

Despite compelling preclinical evidence, several challenges hinder the clinical translation of phytochemicals.

1. Poor Bioavailability

Many phytochemicals suffer from:

- low water solubility
- rapid metabolism
- poor gastrointestinal absorption
- fast systemic clearance

For example:

- Curcumin's bioavailability is extremely low due to rapid glucuronidation.
- Resveratrol undergoes extensive first-pass metabolism.
- EGCG is unstable at physiological ph.

These issues limit their therapeutic efficacy in humans.

2. Variability in Composition and Purity

Plant-derived compounds differ significantly based on:

- extraction method
- plant maturity
- geographical origin
- storage conditions

This variability makes standardization difficult and affects reproducibility of clinical outcomes.

3. Limited High-Quality Clinical Trials

Most evidence comes from laboratory studies. Only a small number of phytochemicals have progressed to advanced clinical trials, and many studies lack:

- large sample sizes
- standardized dosages
- long-term follow-up
- uniform outcome measures

4. Drug–Phytochemical Interactions

Some phytochemicals may:

- interfere with drug metabolism
- inhibit or induce cytochrome P450 enzymes
- affect absorption of chemotherapeutic agents

For example, high doses of EGCG may alter the pharmacokinetics of certain drugs.

5. Dose Optimization

Effective doses in cell or animal studies often exceed what is achievable through diet. There is a need for:

- optimized therapeutic dosing
- encapsulation technologies
- sustained-release formulations

5.3 Future Perspectives

1. Nanotechnology-Based Formulations

Nanoparticles, liposomes, micelles, and polymeric carriers improve solubility, stability, and targeted delivery of phytochemicals. For example:

- curcumin nanoparticles
- resveratrol liposomes
- EGCG-loaded micelles

These approaches significantly enhance therapeutic potential.

2. Combination Therapies

Future research should focus on:

- phytochemical–phytochemical combinations
- phytochemical–drug combinations
- phytochemical–immunotherapy synergy

Such combinations may reduce drug resistance and improve treatment outcomes.

3. Personalized Medicine

Understanding patient-specific factors such as:

- genetic polymorphisms
- tumour subtype
- metabolic profile

may help tailor phytochemical therapy for maximum benefit.

4. Mechanistic Studies and Biomarker Identification

More research is needed to:

- clarify molecular targets
- identify predictive biomarkers
- evaluate long-term safety profiles

This will strengthen clinical translation.

5. Integration Into Clinical Practice

Phytochemicals hold promise as:

- chemo preventive agents
- adjuncts to standard therapy
- supportive care agents to manage side effects

Guidelines for safe and effective use must be developed through rigorous research.

CONCLUSION

Breast cancer continues to impose a major global health burden, driven by rising incidence, tumour heterogeneity, and the persistent challenge of therapy resistance. Although conventional treatments such as chemotherapy, radiotherapy, endocrine therapy, immunotherapy, and targeted therapies have significantly improved patient survival, they remain limited by toxicity, high cost, and reduced efficacy in aggressive cancer subtypes. As a result, research interest has steadily shifted toward identifying novel therapeutic agents that are safe, accessible, multitargeted, and capable of complementing standard therapies.

Dietary phytochemicals fulfil many of these criteria. Extensive preclinical evidence demonstrates that compounds such as curcumin, genistein, resveratrol, EGCG, sulforaphane, quercetin, lycopene, berberine, and withaferin A regulate multiple cancer-related pathways simultaneously. These include key mechanisms such as inhibition of proliferation, induction of apoptosis, suppression of metastasis, attenuation of angiogenesis, modulation of inflammation, reduction of oxidative stress, and epigenetic regulation. Their ability to influence multiple molecular targets—PI3K/Akt/mTOR, NF-κB, MAPK, Wnt/β-catenin, STAT3, Nrf2, and caspase signalling—positions phytochemicals as powerful candidates for integrative breast cancer management. However, despite strong laboratory-based evidence, several barriers still hinder clinical translation. Challenges such as low bioavailability, instability, inconsistent plant-derived formulations, and limited large-scale clinical trials must be addressed. Advances in nanotechnology-based formulations, optimized delivery systems, and combination strategies with existing chemotherapies are promising approaches to overcome these limitations. Future research should concentrate on standardized dosing, biomarker identification, patient-specific responses, and high-quality randomized clinical trials. In conclusion, dietary phytochemicals represent a promising class of anticancer agents with significant potential for breast cancer prevention, therapy enhancement, and long-term disease management. With continued scientific advancements, improved formulations, and clinical validation, phytochemicals may play an increasingly important role as safe, effective, and affordable therapeutic allies in the fight against breast cancer.

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