



NARRATIVE REVIEW

Phytoestrogens and Phytoestrogen-Containing Ayurvedic Botanicals in Breast Cancer: A Narrative Review of Molecular, Preclinical and Clinical Evidence

Sruthi KP¹, Pradeep K²

¹Final Year PG Scholar, Department of Kriyasareera, Govt. Ayurveda College Kannur.

²Asso. Professor, Department of Kriyasareera, Govt. Ayurveda College Kannur.

*Email: karippalasruthi@gmail.com

ARTICLE HISTORY

Received: 24 June 2026

Accepted: 23 September 2026

Available online

Version 1.0: 30 September 2026

Keywords

Phytoestrogens, Breast cancer, Ayurvedic botanicals, *Rasayana*, Estrogen receptors, Soy isoflavones, Integrative oncology

Additional information

Peer review: Publisher thanks Sectional Editor and the other anonymous reviewers for their contribution to the peer review of this work.

Reprints & permissions information is available at <https://keralajournalofayurveda.org/index.php/kja/open-access-policy>

Publisher's Note: All Kerala Govt. Ayurveda College Teacher's Association remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Copyright: © The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited (<https://creativecommons.org/licenses/by/4.0/>).

CITE THIS ARTICLE

Sruthi KP, Pradeep K. Phytoestrogens and Phytoestrogen-Containing Ayurvedic Botanicals in Breast Cancer: A Narrative Review of Molecular, Preclinical and Clinical Evidence. Kerala Journal of Ayurveda. 2026;5(3):46-54.

<https://doi.org/10.55718/kja.626>



Abstract

Phytoestrogens are plant-derived compounds that can interact with estrogen receptors and may exert estrogenic, anti-estrogenic, or context-dependent modulatory effects. Their biological activity varies according to the individual compound, receptor subtype expression, endogenous hormonal environment, concentration, metabolism, and experimental or clinical context. Breast cancer is the most commonly diagnosed cancer among women worldwide, accounting for 2,296,840 new cases (23.8% of all cancers in women) in 2022. Several botanicals used in Ayurveda contain constituents that have been investigated for estrogen-modulating or endocrine-related biological activities; however, the evidence for classifying individual Ayurvedic botanicals as established phytoestrogen sources is variable.

This narrative review examines the available evidence concerning phytoestrogens and selected Ayurvedic botanicals in relation to breast cancer, with particular emphasis on estrogen receptor modulation, receptor-independent signalling pathways, experimental findings in different breast cancer subtypes, dietary phytoestrogen exposure, and the potential relevance of Ayurvedic therapeutic concepts.

Literature was identified from PubMed, Scopus, Google Scholar, ScienceDirect, and selected Ayurvedic sources. Experimental, epidemiological, and clinical evidence was considered alongside classical and contemporary Ayurvedic literature. The evidence was synthesized thematically according to molecular mechanisms, breast cancer subtype, source and formulation of phytoestrogen exposure, and level of evidence.

Available evidence indicates that phytoestrogens may influence breast cancer-related pathways through estrogen receptor-dependent and receptor-independent mechanisms, including pathways involved in cell proliferation, apoptosis, inflammation, oxidative stress, and signal transduction. However, findings are heterogeneous, and effects observed with isolated compounds or experimental models cannot be directly extrapolated to whole herbs or Ayurvedic formulations. Human evidence is stronger for dietary phytoestrogen exposure, particularly soy isoflavones, than for whole Ayurvedic botanicals. Evidence specifically evaluating standardized Ayurvedic preparations in breast cancer patients remains limited.

Future research should evaluate Ayurvedic herbs, individually or in combinations, alongside hormone-modulating drugs through standardised phytochemical, pharmacokinetic, herb-drug interaction, and well-designed clinical studies to establish their safety and potential adjunctive role in breast cancer care.

Introduction

Phytoestrogens are plant-derived polyphenolic compounds structurally similar to 17 β -estradiol and capable of interacting with estrogen receptors (ER).^[1] Depending on receptor subtype distribution, endogenous hormonal milieu, and dose, they may exert estrogenic, anti-estrogenic, or selective modulatory effects. In addition to estrogen receptor (ER)-mediated pathways, phytoestrogens influence multiple cellular signalling networks, including PI3K/Akt, MAPK, NF- κ B, oxidative stress pathways, and apoptosis regulators.^[2]

In Ayurvedic medicine, numerous botanicals used in *Streeroga* (gynaecological disorders) and *Rasayana* therapy contain phytoestrogenic constituents.^[3] Herbs such as *Asparagus racemosus*, *Glycyrrhiza glabra*, *Pueraria tuberosa* etc are traditionally employed for menstrual disorders, fertility support, menopausal symptoms, and systemic rejuvenation. The traditional use of phytoestrogen-containing botanicals in menstrual and gynaecological disorders provides a pharmacological and Ayurvedic rationale for investigating their possible relevance to breast cancer, particularly through estrogen-related pathways.

Breast cancer is the most frequently diagnosed malignancy among women worldwide and remains a leading cause of cancer-related mortality. According to global estimates, approximately 2.3 million new cases are diagnosed annually, accounting for nearly one in four cancers among women.^[4] Despite improvements in early detection and systemic therapy, recurrence, therapeutic resistance, and treatment-related toxicity continue to pose major clinical challenges.^[5]

Breast cancer is a biologically heterogeneous disease, and its management is largely guided by molecular classification. Based on hormone receptor and HER2 expression, tumours are categorised into estrogen receptor (ER)-positive, progesterone receptor (PR)-positive, HER2-positive, and triple-negative breast cancer (TNBC) subtypes.^[6] Approximately 70–80% of breast cancers are ER-positive and depend partly on estrogen signalling for tumour growth. Endocrine therapies such as tamoxifen and aromatase inhibitors significantly improve survival in these patients, although resistance frequently develops. In contrast, TNBC lacks ER, PR, and HER2 expression and is associated with aggressive behaviour and limited targeted treatment options.^[7]

However, the implications of these phytoestrogen-containing herbs in hormone-dependent malignancies, particularly ER-positive breast cancer, remain insufficiently explored.^[8] Experimental studies suggest that phytoestrogens may exhibit both tumour-inhibitory and proliferative effects depending on dose, receptor expression, and hormonal context.^[9] These conflicting findings highlight the need for careful evaluation when considering their therapeutic role in breast cancer. This review aims to evaluate receptor-dependent effects of phytoestrogenic herbs in breast cancer and propose a subtype-guided integrative framework for their potential clinical application.

Methodology

This study was conducted as a narrative review examining phytoestrogenic compounds, Ayurvedic herbs containing estrogen-modulating constituents, and their relevance in breast cancer biology.

Literature searches were performed using databases including PubMed, Scopus, and Google Scholar. Keywords included combinations of *phytoestrogens*, *breast cancer*, *estrogen receptor*, *Ayurveda*, *Rasayana*, *herbal phytoestrogens*, and *molecular subtype*. Both experimental and clinical studies investigating estrogen receptor modulation, signalling pathways, and epidemiological associations between phytoestrogen exposure and breast cancer outcomes were included. Articles from 2015 to 2025 were included in this research.

The retrieved literature was screened initially on the basis of title and abstract, followed by evaluation of potentially relevant full-text articles. Relevant references identified from the reference lists of included articles were also considered where appropriate.

Classical Ayurvedic texts and modern Ayurvedic pharmacological sources were also reviewed to identify herbs traditionally used in *Streeroga* and *Rasayana* therapy that possess potential phytoestrogenic activity.

The retrieved literature was synthesized and categorized into thematic areas including phytoestrogen-containing Ayurvedic herbs, molecular mechanisms of action, subtype-specific effects in breast cancer, Ayurvedic conceptual correlations, and considerations for clinical integration. The selection process is presented in Diagram 1.

Results

Phytoestrogen-Containing Herbs in Ayurveda

The Ayurvedic pharmacopoeia includes several botanicals traditionally used in gynaecological disorders, reproductive health, menopausal symptoms, and *Rasayana* therapy that contain compounds with reported estrogen-modulating activity. Commonly cited botanicals include *Asparagus racemosus* (*Shatavari*), *Glycine max* (soy), *Trigonella foenum-graecum* (fenugreek), *Pueraria tuberosa* (*Vidarikanda*), *Foeniculum vulgare* (fennel), *Glycyrrhiza glabra* (*Yashtimadhu*), *Saraca asoca* (*Ashoka*), *Linum usitatissimum* (flaxseed), *Aloe barbadensis* (*Kumari*), *Tribulus terrestris* (*Gokshura*), and *Crocus sativus* (*Kumkuma*). These plants contain diverse phytoconstituents, including isoflavones, lignans, flavonoids, and steroidal saponins.

Soy and flaxseed are primarily consumed as foods, and evidence regarding their breast-cancer-related effects largely derives from dietary intake, epidemiological studies, and nutritional interventions. In contrast, Ayurvedic botanicals may be administered therapeutically as powders, decoctions, extracts, or polyherbal formulations, with substantially different doses, phytochemical concentrations, bioavailability, and pharmacokinetic profiles.^[8]

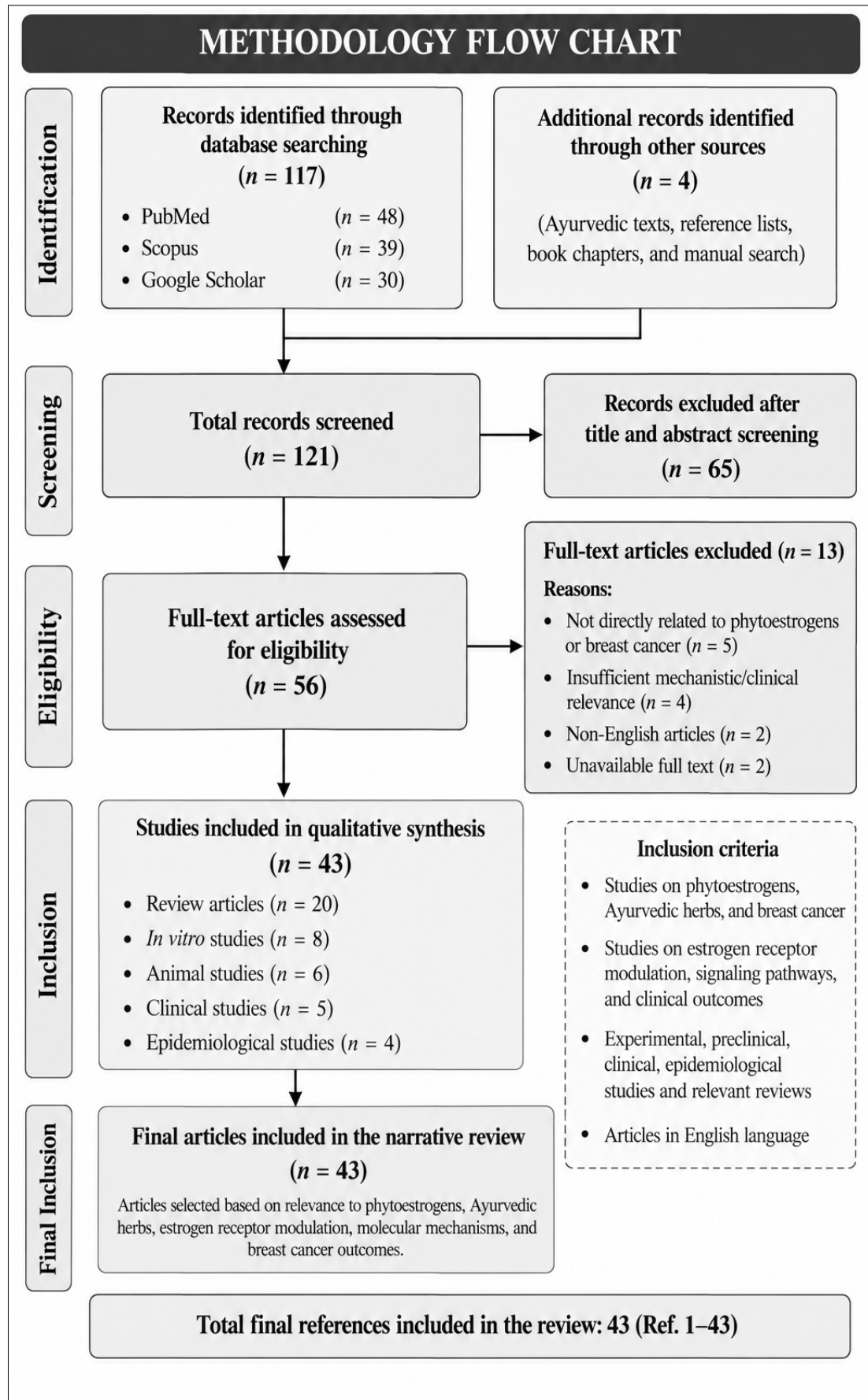


Diagram 1. Methodology flow chart.

The distinction between whole botanicals and their isolated constituents is particularly important. Demonstration of estrogen receptor binding or an anticancer effect by an isolated phytochemical does not establish that the corresponding whole herb or Ayurvedic formulation will produce the same biological effect. Whole botanicals contain multiple constituents whose interactions may be additive, synergistic, or antagonistic, and differences in extraction method, dose, formulation, bioavailability, metabolism, and pharmacokinetics may substantially influence their biological effects.

Furthermore, evidence for estrogen-receptor binding or anticancer activity of isolated phytochemicals cannot be directly extrapolated to the corresponding whole herb or Ayurvedic preparation, whose multiple constituents may act synergistically or antagonistically. Traditional use in reproductive or menopausal disorders provides a basis for therapeutic relevance but does not establish anticancer efficacy; evidence specifically evaluating whole Ayurvedic botanicals or standardised formulations in breast cancer remains limited compared with the evidence for dietary phytoestrogens and isolated phytochemicals.

Table 1. Phytoestrogen-containing herbs, Ayurvedic therapeutic relevance and evidence related to breast cancer

Herb	Major phytoestrogenic constituents	Ayurvedic therapeutic relevance	ER-related activity	Breast-cancer-specific evidence	Other molecular targets/pathways	Evidence level
<i>Asparagus racemosus</i> (Shatavari)	Steroidal saponins (shatavarins), sarsasapogenin, flavonoids	Traditionally used in female reproductive health, <i>Rasayana</i> and <i>Stanyajanana</i> indications	Estrogenic activity reported; ER-subtype specificity remains incompletely characterized	Root extracts have demonstrated antineoplastic/chemopreventive effects in experimental mammary cancer models. More recent studies report inhibition of MDA-MB-231 TNBC cells, with reduced viability, G1 arrest and apoptosis. ^[10]	Apoptosis, cell-cycle regulation, oxidative stress; AKT1/ERBB2-related signalling suggested	In vitro and in vivo; no clinical breast-cancer evidence
<i>Trigonella foenum-graecum</i> (Fenugreek)	Diosgenin, flavonoids, alkaloids, isoflavones	Traditionally used for digestive, metabolic, lactation and reproductive indications	Estrogenic activity demonstrated in experimental systems; ER-mediated effects reported, but receptor selectivity is not firmly established	Multiple studies using MCF-7 and SK-BR-3 cells report dose-dependent cytotoxicity, apoptosis, inhibition of migration/adhesion and modulation of p53-related pathways. ^[11]	p53, Bax/Bcl-2, caspases, NF-κB, STAT3, mitochondrial pathways	Substantial in vitro; some in vivo; no established clinical breast-cancer evidence
<i>Pueraria tuberosa</i> (Vidarikanda)	Puerarin and other isoflavonoids/isoflavone-related compounds	Traditionally associated with <i>Balya</i> , <i>Brimhana</i> and <i>Rasayana</i> applications	Potential estrogen-receptor interaction; subtype specificity remains uncertain	<i>P. tuberosa</i> constituents and extracts have shown cytotoxic/antiproliferative activity against MCF-7 cells; additional studies involve MDA-MB-231 models. ^[12]	Apoptosis, oxidative stress, mitochondrial pathways	In vitro; limited in vivo; no clinical evidence
<i>Foeniculum vulgare</i> (Shatapushpa/Fennel)	Anethole, flavonoids and phenolic constituents	Traditionally used in digestive and female reproductive indications, including menstrual and lactation-related applications	Estrogenic activity has been reported; direct ER-binding evidence remains limited	Breast-cancer-specific experimental studies include breast-cancer cell models and investigations of antiproliferative mechanisms. HSP90-related activity has also been reported. Molecular-docking studies provide additional mechanistic hypotheses but should not be treated as efficacy evidence. ^[13]	HSP90, oxidative stress, apoptosis and proliferation-related pathways	In vitro and in silico; no clinical anticancer evidence
<i>Glycyrrhiza glabra</i> (Yashtimadhu)	Liquiritigenin, isoliquiritigenin, glycyrrhizin, other flavonoids	Traditionally used in several inflammatory, gastrointestinal, respiratory and <i>Rasayana</i> -related indications	Liquiritigenin has ERβ-selective activity in experimental systems	Multiple licorice constituents have been studied in breast-cancer models. Recent work has investigated licoflavanone in breast-cancer cells, while other studies have examined estrogen-related and aromatase-associated mechanisms. ^[14,15]	Aromatase, MAPK, inflammatory signalling, mitochondrial bioenergetics, apoptosis	In vitro; limited in vivo; no clinical breast-cancer efficacy evidence

<i>Linum usitatissimum</i> (Atasi/flaxseed)	Secoisolariciresinol diglucoside (SDG), lignans, α -linolenic acid	Dietary/oilseed drug;	Lignan metabolites such as enterolactone interact with estrogen receptors and may show relative ER β preference	One of the better-studied plant foods in breast cancer. Studies report effects on proliferation, apoptosis, HER2 expression and biomarkers. Observational studies suggest associations with reduced breast-cancer risk/mortality, while clinical trials remain limited and heterogeneous. ^[16]	Aromatase modulation, apoptosis, proliferation, angiogenesis and inflammatory pathways	In vitro, in vivo, observational and limited clinical evidence
<i>Aloe vera</i> (Kumari)	Aloe-emodin, emodin, phytosterols, anthraquinones, polysaccharides	Traditionally used in female reproductive and gastrointestinal indications and in several external/internal therapeutic applications	Phytoestrogenic potential reported; aloe-emodin can influence ER α -related signalling	Multiple studies demonstrate antiproliferative and apoptotic activity against MCF-7 and other breast-cancer models. Aloe-emodin has been reported to suppress ER α protein stability and induce apoptosis. ^[17]	ER α /HSP90, Bcl-2/Bax, p21, miRNA-mediated pathways, apoptosis	Substantial in vitro; limited in vivo; no clinical breast-cancer efficacy evidence
<i>Tribulus terrestris</i> (Gokshura)	Steroidal saponins including protodioscin	Traditionally used predominantly for urinary-system indications and as <i>Mutrala</i> ;	Direct ER binding is not well established; endocrine effects may contribute to biological activity	Extracts and saponin fractions have demonstrated dose-dependent inhibition of MCF-7 breast-cancer cell viability and induction of apoptosis, including DNA fragmentation and caspase activation. ^[18]	Apoptosis, caspases, oxidative stress and endocrine-related signalling	In vitro; limited in vivo; no clinical evidence

Molecular Mechanisms of Phytoestrogens

Estrogen Receptor Modulation

Phytoestrogens may function as selective estrogen receptor modulators (SERMs), interacting with ER α and ER β . ER α activation is generally associated with proliferative signalling in breast tissue, whereas ER β signalling has been linked to anti-proliferative and differentiating effects. The relative ER α /ER β expression ratio, therefore, plays a key role in determining biological outcomes.^[28]

Dose-Dependent Biphasic Effects

Many phytoestrogens exhibit biphasic or hormetic responses. At low concentrations, particularly in low estrogen environments, certain compounds may stimulate proliferation in ER-positive cells. In contrast, higher concentrations often induce cell cycle arrest, apoptosis, and inhibition of proliferative signalling pathways.^[29] This concentration-dependent behaviour contributes to the variable findings reported in experimental and clinical studies.^[30]

ER-Independent Pathways

Phytoestrogens also regulate several ER-independent signalling pathways. These include modulation of PI3K/Akt/mTOR, MAPK/ERK, and NF- κ B signalling, which influence cell survival, inflammation, and tumour progression. They may also alter oxidative stress responses, apoptosis regulators, epigenetic mechanism such as DNA methylation and histone modification. Through these mechanisms, phytoestrogens may exert anti-inflammatory and anti-proliferative effects even in cells lacking functional estrogen receptors.^[31]

Modulation of Estrogen Metabolism and Aromatase Activity

Several phytoestrogens can modulate the activity of cytochrome P450 enzymes such as CYP1A1 and CYP1B1, which are involved in the metabolic conversion of estrogens into various hydroxylated metabolites. By altering the activity of these enzymes, phytoestrogens may shift estrogen metabolism toward pathways that generate less genotoxic metabolites. Compounds such as resveratrol, genistein, and quercetin have been reported to interfere with aryl hydrocarbon receptor (AhR) signalling and suppress the expression of CYP1A1 and CYP1B1.^[32]

Phytoestrogens may also influence other estrogen-metabolising enzymes such as catechol-O-methyltransferase (COMT), which participates in the detoxification of catechol estrogen metabolites. In addition, some phytoestrogens have been shown to inhibit aromatase, the enzyme responsible for the peripheral conversion of androgens into estrogens. Through these effects on estrogen synthesis and metabolism, phytoestrogens can indirectly influence the hormonal microenvironment of breast tissue and potentially affect tumour development and progression.^[2]

Effects in ER-Positive Breast Cancer

Epidemiological studies, particularly from East Asian populations with long-term dietary soy intake, suggest that higher isoflavone consumption may be associated with reduced breast cancer recurrence and improved survival among survivors, including those with ER-positive disease.^[33]

The diverse experimental and epidemiological findings regarding the effects of phytoestrogens in breast cancer are summarized in Table 2. These studies demonstrate both protective and context-dependent proliferative effects depending on dose, exposure timing, hormonal milieu, and tumour characteristics.

Preclinical studies demonstrate that phytoestrogens can inhibit proliferation, induce apoptosis, and suppress tumour-promoting signalling pathways in ER-positive breast cancer models. However, certain isoflavones such as genistein have been shown to stimulate proliferation at low concentrations in experimental models under low estrogen conditions.

Effects in Triple-Negative and ER-Negative Breast Cancer

In ER-negative and triple-negative breast cancers, phytoestrogens exert biological effects primarily through ER-independent mechanisms.

Experimental studies indicate that several phytoestrogenic compounds inhibit NF-κB signalling, suppress epithelial-mesenchymal transition, and induce apoptosis in TNBC cell lines. Additional reported effects include inhibition of tumour cell migration, suppression of metastatic potential, and modulation of inflammatory signalling within the tumour microenvironment.^[43]

However, most evidence currently derives from in vitro or animal studies, and clinical data evaluating these effects in TNBC patients remain limited.

Table. 2 Summary of studies showing proliferative and antiproliferative effect of phytoestrogenic compounds.

Phytoestrogen	Study Model	Mechanism / Target	Observed Effect on Breast Cancer	Key Findings
Genistein ^[34]	ER-positive breast cancer cell lines	ER modulation, Akt signalling, NF-κB inhibition	Biphasic effect	Low concentrations stimulated proliferation under low estrogen conditions; higher concentrations showed anti-proliferative effects
Genistein ^[35]	Rodent models of mammary carcinogenesis	Hormonal modulation during mammary development	Protective (early exposure)	Early-life exposure reduced susceptibility to DMBA-induced mammary tumours
Genistein ^[36]	Rat mammary tumour models	Estrogen receptor signalling	Adverse effect in some studies	Increased tumour multiplicity and tumour size in estrogen-dependent tumours
Resveratrol ^[37]	DMBA-induced mammary carcinogenesis in rats	PI3K inhibition, NF-κB suppression	Protective	Reduced tumour incidence and increased tumour latency
Resveratrol ^[38]	Breast cancer cell lines	ERα-associated signalling, MAPK pathway	Anti-proliferative	Inhibited ERα-mediated PI3K activity and NF-κB signalling
Daidzein ^[39]	Rodent mammary tumour models	ER modulation	Protective	Inhibited DMBA-induced mammary tumours and increased tumour latency
Quercetin ^[40]	Chemically induced tumour models	CYP450 modulation, COMT interaction	Mixed effects	Demonstrated tumour inhibition in some studies but enhanced estrogen-induced tumorigenesis in others
Isoflavones (dietary) ^[33]	Epidemiological studies in East Asian populations	Long-term dietary exposure	Protective association	Higher dietary soy intake linked with reduced recurrence and improved survival in breast cancer survivors
Multiple phytoestrogens ^[41]	Gene expression studies (MCF7 cells)	MAPK, apoptosis pathways	Modulatory effects	Altered expression of genes regulating cell growth, differentiation, and apoptosis
Multiple phytoestrogens ^[42]	Enzyme studies	CYP1A1, CYP1B1, COMT	Metabolic modulation	Influenced estrogen metabolism and balance of estrogen metabolites

These findings suggest that the biological effects of phytoestrogens in ER-positive breast cancer are strongly influenced by dose, hormonal environment, and receptor subtype expression.

Discussion

The present review highlights the complex and context-dependent nature of phytoestrogen activity in breast cancer biology. The biological effects of these compounds are not uniform but are influenced by multiple interacting factors, including receptor subtype distribution, endogenous hormonal milieu, dosage, formulation, and metabolic transformation.

A central determinant of phytoestrogen activity is the balance between estrogen receptor subtypes, particularly ER α and ER β . ER α signalling is primarily associated with proliferative responses in breast epithelial cells, whereas ER β has been reported to exert anti-proliferative and differentiating effects. Many phytoestrogens, particularly isoflavones such as genistein and daidzein, exhibit a preferential binding affinity for ER β over ER α . Through this selective receptor interaction, phytoestrogens may function as selective estrogen receptor modulators, producing estrogenic or anti-estrogenic effects depending on receptor distribution and cellular context. The relative ER α /ER β expression ratio within tumour tissue, therefore, becomes an important determinant of cellular response.^[28]

Another key factor influencing biological activity is the dose-dependent and, in some phytoestrogens, biphasic response observed in experimental studies. At lower concentrations, particularly under conditions of low endogenous estrogen levels, certain phytoestrogens may act as weak estrogen receptor agonists by occupying unbound estrogen receptors and producing mild estrogenic signalling. At higher concentrations, some phytoestrogens may compete with endogenous estradiol for receptor binding and, depending on their receptor selectivity and cellular context, may preferentially influence ER β -mediated pathways and modulate ER α -associated proliferative signalling. However, this pattern is not consistent across all phytoestrogens, as their effects vary according to the specific compound, concentration, estrogenic environment, receptor expression profile, and target tissue. Such context- and dose-dependent responses may contribute to the variability observed across experimental and clinical studies and underscore the importance of considering dose and biological context when interpreting their therapeutic potential.^[30]

The pharmacokinetics and bioavailability of phytoestrogens represent another critical aspect in evaluating their clinical relevance. Following oral ingestion, many phytoestrogens are absorbed in the intestine, metabolised by gut microbiota, and subsequently conjugated in the liver to glucuronide and sulfate derivatives before entering systemic circulation. Isoflavones such as genistein and daidzein typically reach peak plasma concentrations within 4–8 hours after ingestion, with elimination half-lives ranging between approximately 6–10 hours. Dietary intake of soy-based phytoestrogens has been shown to produce plasma concentrations of approximately 0.1–5 μ M, levels that overlap with those demonstrating biological activity in several experimental models. Additionally, microbial metabolism can convert daidzein into equol, a metabolite with a stronger affinity for ER β , although this conversion occurs only in a subset of individuals depending on gut microbiota composition. Such inter-individual metabolic variability may partly explain differences in clinical outcomes reported in epidemiological studies.^[31]

Nevertheless, it is important to recognise that many anti-proliferative effects observed in experimental systems occur at concentrations higher than those typically achieved through dietary exposure alone. Therefore, the therapeutic effects of phytoestrogen-containing botanicals may depend not only on isolated compounds but also on complex phytochemical matrices, formulation characteristics, and long-term dietary patterns that influence systemic signalling networks.

Within the Ayurvedic framework, the use of phytoestrogen-containing herbs is understood through a broader therapeutic paradigm. Many of these botanicals are classified as *Rasayana*, which emphasises systemic rejuvenation, tissue nourishment, and restoration of physiological balance rather than direct hormonal stimulation. This perspective differs from reductionist pharmacological approaches that focus primarily on isolated receptor interactions. Instead, *Rasayana* therapy aims to modulate systemic metabolic processes, enhance tissue resilience, and maintain homeostasis across multiple physiological systems.

Ayurveda also emphasizes individualized treatment strategies based on *Prakriti* (constitutional type), *Doṣha* balance, and *Agni* (metabolic capacity).^[44] Such personalized therapeutic principles conceptually parallel modern precision oncology approaches, where treatment decisions are increasingly guided by molecular tumour characteristics and patient-specific biological factors. In this context, phytoestrogenic herbs may serve as modulatory agents within a broader integrative therapeutic framework rather than functioning as direct endocrine substitutes.

Classical Ayurvedic descriptions associating abnormal tissue growth with *Kapha* and *Meda* dysregulation further highlight the importance of correcting metabolic imbalance before administering *Rasayana* therapies. This staged therapeutic approach may theoretically reduce potential risks related to proliferative stimulation by first addressing underlying metabolic disturbances and ensuring appropriate physiological regulation.^[45] In addition, Ayurvedic pharmacology recognises the concept of appropriate timing of drug administration (*Aushadha Sevana Kala*), administering medicines in relation to meals or physiological states to optimise their action and absorption.^[46]

Ayurvedic clinical decision-making also incorporates structured diagnostic frameworks such as the tenfold clinical examination (*Dasavidha pareeksha*) and the therapeutic model known as *Chikitsa Chatushtaya*, which considers the physician, medicine, patient, and supportive care as essential components of successful treatment. These principles emphasise individualised assessment of constitutional type, metabolic strength, disease stage, and tissue status before initiating therapy.^[47] When interpreted in a contemporary biomedical context, such individualised therapeutic planning shows conceptual parallels with modern precision medicine approaches, where treatment strategies are tailored according to molecular tumour characteristics and patient-specific biological factors. Future research integrating molecular oncology with traditional Ayurvedic principles may provide a more comprehensive understanding of how phytoestrogen-containing botanicals can be safely and effectively incorporated into integrative cancer care strategies.

Future Research Gaps

Despite growing interest in phytoestrogens, significant research gaps remain. Most studies focus on isolated phytochemicals instead of whole herbs or traditional Ayurvedic formulations. Future research should explore the pharmacological effects of complex herbal combinations and clarify dose-response relationships under relevant hormonal conditions, particularly differences between premenopausal and postmenopausal environments.

Understanding the dynamics of estrogen receptors and investigating phytoestrogen effects on non-ER signalling pathways could shed light on their role in various breast cancer subtypes. Additionally, well-designed clinical trials assessing standardised Ayurvedic formulations in molecularly characterised breast cancer populations with subtype stratification and long-term safety monitoring are crucial.

It's also important to study potential herb-drug interactions when phytoestrogens are used alongside endocrine therapies like Tamoxifen and Aromatase Inhibitors, as they may affect treatment efficacy and safety. Systematic evaluation of these interactions is essential for their safe integration into oncology care.

Conclusion

Phytoestrogens represent a biologically complex group of compounds with context-dependent effects in breast cancer. Their actions may be tumour-promoting or tumour-inhibitory depending on dose, endocrine environment, receptor subtype distribution, and molecular tumour characteristics.

Several Ayurvedic herbs containing phytoestrogenic constituents demonstrate potential therapeutic relevance, particularly within traditional *Rasayana* frameworks that emphasise systemic regulation and individualised therapy.

Integration of molecular breast cancer classification with Ayurvedic therapeutic principles may provide a promising direction for future integrative oncology research.

Source of funding- None

This work did not receive any specific grants from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations: The authors declare no conflicts of interest.

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declaration of Generative AI and AI-assisted technologies in the writing process

AI-based language assistance tools (ChatGPT and Paperpal) were used only for grammar and language refinement. All intellectual content, analyses, and conclusions are those of the authors.

References

1. Patra S, Gorai S, Pal S, Ghosh K, Pradhan S, Chakrabarti S. A review on phytoestrogens: Current status and future direction. *Phytotherapy Research*. 2023;37(7):3097–120. doi:10.1002/ptr.7861
2. Basu P, Maier C. Phytoestrogens and breast cancer: In vitro anticancer activities of isoflavones, lignans, coumestans, stilbenes and their analogs and derivatives. *Biomedicine and Pharmacotherapy*. Elsevier Masson SAS; 2018. p. 1648–66. doi:10.1016/j.biopha.2018.08.100 PubMed PMID: 30257383.
3. Kulkarni P. Phytoestrogens Medicinal Herbs - Safe and Effective Alternative to Hormone Replacement Therapy in Menopausal Syndrome. *JOURNAL OF RESEARCH IN TRADITIONAL MEDICINE*. 2017;2(5):147–50. doi:10.21276/jrtm.2016/278
4. Zhang Y, Ji Y, Liu S, Li J, Wu J, Jin Q, et al. Global burden of female breast cancer: new estimates in 2022, temporal trend and future projections up to 2050 based on the latest release from GLOBOCAN. *Journal of the National Cancer Center*. 2025;5(3):287–96. doi:10.1016/j.jncc.2025.02.002
5. Zafar A, Khatoon S, Khan MJ, Abu J, Naeem A. Advancements and limitations in traditional anti-cancer therapies: a comprehensive review of surgery, chemotherapy, radiation therapy, and hormonal therapy. *Discover oncology*. 2025;16(1):607. doi:10.1007/s12672-025-02198-8 PubMed PMID: 40272602.
6. Orrantia-Borunda E, Anchondo-Nuñez P, Acuña-Aguilar LE, Gómez-Valles FO, Ramírez-Valdespino CA. Subtypes of Breast Cancer. In: *Breast Cancer*. Exon Publications; 2022. p. 31–42. doi:10.36255/exon-publications-breast-cancer-subtypes
7. Łukasiewicz S, Czelelewski M, Forma A, Baj J, Sitarz R, Stanisławek A. Breast Cancer—Epidemiology, Risk Factors, Classification, Prognostic Markers, and Current Treatment Strategies—An Updated Review. *Cancers (Basel)*. 2021;13(17):4287. doi:10.3390/cancers13174287
8. Shanmugaloga S, Shilpa P N. Phytoestrogens: Unlocking the Power of Plant Based Estrogens. *Journal of Ayurveda and Integrated Medical Sciences*. 2024;9(6):164–74. doi:10.21760/jaaims.9.6.25
9. Swathi Krishna S, Kuriakose BB, Lakshmi PK. Effects of phytoestrogens on reproductive organ health. *Arch Pharm Res*. 2022;45(12):849–64. doi:10.1007/s12272-022-01417-y
10. Prasad K, Saggam A, Guruprasad KP, Tillu G, Patwardhan B, Satyamoorthy K. Molecular mechanisms of *Asparagus racemosus* Willd. and *Withania somnifera* (L.) Dunal as chemotherapeutic adjuvants for breast cancer treatment. *J Ethnopharmacol*. 2024;331:118261. doi:10.1016/j.jep.2024.118261
11. Alrumaihi FA, Khan MA, Allemaille KS, Alsahli MA, Almatroudi A, Younus H, et al. Methanolic Fenugreek Seed Extract Induces p53-Dependent Mitotic Catastrophe in Breast Cancer Cells, Leading to Apoptosis. *J Inflamm Res*. 2021;Volume 14:1511–35. doi:10.2147/JIR.S300025
12. Bharti R, Chopra BS, Raut S, Khatri N. *Pueraria tuberosa*: A Review on Traditional Uses, Pharmacology, and Phytochemistry. *Front Pharmacol*. 2021;11. doi:10.3389/fphar.2020.582506
13. Kaur B, Rolta R, Salaria D, Kumar B, Fadare OA, da Costa RA, et al. An In Silico Investigation to Explore Anti-Cancer Potential of *Foeniculum vulgare* Mill. Phytoconstituents for the Management of Human Breast Cancer. *Molecules*. 2022;27(13):4077. doi:10.3390/molecules27134077
14. Hajirahimkhan A, Howell C, Bartom ET, Dong H, Lantvit DD, Xuei X, et al. Breast cancer prevention with liquiritigenin from licorice through the inhibition of aromatase and protein biosynthesis in high-risk women's breast tissue. *Sci Rep*. 2023;13(1):8734. doi:10.1038/s41598-023-34762-z

15. Wahab S, Annadurai S, Abullais SS, Das G, Ahmad W, Ahmad MF, et al. Glycyrrhiza glabra (Licorice): A Comprehensive Review on Its Phytochemistry, Biological Activities, Clinical Evidence and Toxicology. *Plants*. 2021;10(12):2751. doi:10.3390/plants10122751
16. Flower G, Fritz H, Balneaves LG, Verma S, Skidmore B, Fernandes R, et al. Flax and Breast Cancer. *Integr Cancer Ther*. 2014;13(3):181–92. doi:10.1177/1534735413502076
17. Huang PH, Huang CY, Chen MC, Lee YT, Yue CH, Wang HY, et al. Emodin and Aloe-Emodin Suppress Breast Cancer Cell Proliferation through ER α Inhibition. *Evidence-Based Complementary and Alternative Medicine*. 2013;2013:1–12. doi:10.1155/2013/376123
18. Patel A, Soni A, Siddiqi NJ, Sharma P. An insight into the anticancer mechanism of Tribulus terrestris extracts on human breast cancer cells. *3 Biotech*. 2019;9(2):58. doi:10.1007/s13205-019-1585-z
19. Pandey AR, Kurkute P, Tyagi B, Pundir A. A comprehensive review on role of phytoconstituents from the roots of Asparagus racemosus (Queen of Herbs). *Phytomedicine Plus*. 2026;6(1):100916. doi:10.1016/j.phyplu.2025.100916
20. Intharuksa A, Arunotayanun W, Na Takuathung M, Chaichit S, Prasansuklab A, Chaikhong K, et al. Daidzein and Genistein: Natural Phytoestrogens with Potential Applications in Hormone Replacement Therapy. *Int J Mol Sci*. 2025;26(14):6973. doi:10.3390/ijms26146973
21. Bhat KM, Nagamma T, Konuri A. Medicinal value of Phytoestrogens in Trigonella foenum-graecum L (Fenugreek) - Review. *Biomedical and Pharmacology Journal*. 2023;16(4):1885–95. doi:10.13005/bpj/2768
22. Satpathy S, Patra A, Hussain MD, Kazi M, Aldughaim MS, Ahirwar B. A fraction of Pueraria tuberosa extract, rich in antioxidant compounds, alleviates ovariectomized-induced osteoporosis in rats and inhibits growth of breast and ovarian cancer cells. *PLoS One*. 2021;16(1):e0240068. doi:10.1371/journal.pone.0240068
23. Lee HW, Lim HJ, Jun JH, Lim HS, Lee MS. Fennel (Foeniculum vulgare) on management of menopausal symptoms. *Medicine*. 2018;97(13):e0223. doi:10.1097/MD.00000000000010223
24. Hasan MdK, Ara I, Mondal MSA, Kabir Y. Phytochemistry, pharmacological activity, and potential health benefits of Glycyrrhiza glabra. *Heliyon*. 2021;7(6):e07240. doi:10.1016/j.heliyon.2021.e07240
25. Imran M, Ahmad N, Anjum FM, Khan MK, Mushtaq Z, Nadeem M, et al. Potential protective properties of flax lignan secoisolariciresinol diglucoside. *Nutr J*. 2015;14(1):71. doi:10.1186/s12937-015-0059-3
26. Kumar S, Kalita S, Basumatary IB, Kumar S, Ray S, Mukherjee A. Recent advances in therapeutic and biological activities of Aloe vera. *Biocatal Agric Biotechnol*. 2024;57:103084. doi:10.1016/j.bcab.2024.103084
27. Ghanbari A, Akhshi N, Nedaei SE, Mollica A, Aneva IY, Qi Y, et al. Tribulus terrestris and female reproductive system health: A comprehensive review. *Phytomedicine*. 2021;84:153462. doi:10.1016/j.phymed.2021.153462
28. Oseni T, Patel R, Pyle J, Jordan V. Selective Estrogen Receptor Modulators and Phytoestrogens. *Planta Med*. 2008;74(13):1656–65. doi:10.1055/s-0028-1088304
29. Jodynis-Liebert J, Kujawska M. Biphasic Dose-Response Induced by Phytochemicals: Experimental Evidence. *J Clin Med*. 2020;9(3):718. doi:10.3390/jcm9030718
30. Lecomte S, Demay F, Ferrière F, Pakdel F. Phytochemicals Targeting Estrogen Receptors: Beneficial Rather Than Adverse Effects? *Int J Mol Sci*. 2017;18(7):1381. doi:10.3390/ijms18071381
31. Soheli M. Breaking Barriers; Phytoestrogens in the Fight Against Triple-Negative Breast Cancer: A Comprehensive Review. *Med Res Rev*. 2025;45(4):1211–50. doi:10.1002/med.22107
32. Lephart ED. Modulation of Aromatase by Phytoestrogens. *Enzyme Res*. 2015;2015:1–11. doi:10.1155/2015/594656
33. Yang J, Shen H, Mi M, Qin Y. Isoflavone Consumption and Risk of Breast Cancer: An Updated Systematic Review with Meta-Analysis of Observational Studies. *Nutrients*. 2023;15(10):2402. doi:10.3390/nu15102402
34. Rajah TT, Du N, Drews N, Cohn R. Genistein in the Presence of 17 β -Estradiol Inhibits Proliferation of ER β Breast Cancer Cells. *Pharmacology*. 2009;84(2):68–73. doi:10.1159/000226123
35. Hilakivi-Clarke L, Onojafe I, Raygada M, Cho E, Skaar T, Russo I, et al. Prepubertal exposure to zearalenone or genistein reduces mammary tumorigenesis. *Br J Cancer*. 1999;80(11):1682–8. doi:10.1038/sj.bjc.6690584
36. Yang X, Yang S, McKimmey C, Liu B, Edgerton SM, Bales W, et al. Genistein induces enhanced growth promotion in ER-positive/erbB-2-overexpressing breast cancers by ER-erbB-2 cross talk and p27/kip1 downregulation. *Carcinogenesis*. 2010;31(4):695–702. doi:10.1093/carcin/bgq007
37. Banerjee S, Bueso-Ramos C, Aggarwal BB. Suppression of 7,12-dimethylbenz(a)anthracene-induced mammary carcinogenesis in rats by resveratrol: role of nuclear factor-kappaB, cyclooxygenase 2, and matrix metalloproteinase 9. *Cancer Res*. 2002;62(17):4945–54. PubMed PMID: 12208745.
38. Hu C, Liu Y, Teng M, Jiao K, Zhen J, Wu M, et al. Resveratrol inhibits the proliferation of estrogen receptor-positive breast cancer cells by suppressing EZH2 through the modulation of ERK1/2 signaling. *Cell Biol Toxicol*. 2019;35(5):445–56. doi:10.1007/s10565-019-09471-x
39. Liu X, Suzuki N, Laxmi YRS, Okamoto Y, Shibutani S. Anti-breast cancer potential of daidzein in rodents. *Life Sci*. 2012;91(11–12):415–9. doi:10.1016/j.lfs.2012.08.022
40. Mohos V, Fliszár-Nyúl E, Ungvári O, Kuffa K, Needs PW, Kroon PA, et al. Inhibitory Effects of Quercetin and Its Main Methyl, Sulfate, and Glucuronic Acid Conjugates on Cytochrome P450 Enzymes, and on OATP, BCRP and MRP2 Transporters. *Nutrients*. 2020;12(8):2306. doi:10.3390/nu12082306
41. Helferich WG, Andrade JE, Hoagland MS. Phytoestrogens and breast cancer: a complex story. *Inflammopharmacology*. 2008;16(5):219–26. doi:10.1007/s10787-008-8020-0
42. Wagner J, Jiang L, Lehmann L. Phytoestrogens Modulate the Expression of 17 α -Estradiol Metabolizing Enzymes in Cultured MCF-7 Cells. In: 2008. p. 625–32. doi:10.1007/978-0-387-69080-3_65
43. Soheli M. Breaking Barriers; Phytoestrogens in the Fight Against Triple-Negative Breast Cancer: A Comprehensive Review. *Med Res Rev*. 2025;45(4):1211–50. doi:10.1002/med.22107
44. T Sreekumar. Ashtanga hridaya sootrasthana 1. Updated 4th edition. Vol. 1. Thrissur : Publication Department Harisree Hospital; 2013. 283 p.
45. Institute of Ayurveda and Integrative Medicine. Vedotpatti <https://vedotpatti.in/samhita/Vag/ehrudayam/?mod=read> Accessed 05 September 2026. e-Vagbhata: Ashtanga Hrudaya.
46. T Sreekumar. Ashtanga hridata Sootrasthana 1. Revised 4th edition. Vol. 1. Thrissur: publication department Harisree hospital; 2013. 300–303 p.
47. T Sreekumar. Ashtanga hridaya Sootrasthana 1. revised 4th edition. Vol. 1. Thrissur: Publication Department Harisree Hospital; 2013. 56–58 p.

§§§