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REVIEW ARTICLE

PHYTOESTROGENS AND HORMONAL BALANCE: ENDOCRINE MODULATION, BENEFITS, AND DISRUPTIVE EFFECTS

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ABSTRACT

Phytoestrogens are naturally occurring bioactive compounds that resemble endogenous estrogens, especially estradiol, in both structure and function. These compounds are commonly present in dietary sources such as flaxseeds, soybeans, legumes, and whole-grain products. They have been extensively studied for their ability to influence endocrine system function. As selective estrogen receptor modulators (SERMs), phytoestrogens show dual activity, acting either as estrogenic or anti-estrogenic depending on the target tissue, receptor binding affinity, and individual hormonal profiles. Their potential health benefits include alleviating menopausal symptoms, enhancing bone health, providing cardiovascular protection, and supporting metabolic regulation. Specific bioactive compounds, such as lignans, isoflavones, coumestans, and stilbenes, have demonstrated potential in reducing the risks of osteoporosis, cardiovascular disease, and insulin resistance. However, despite these benefits, concerns about their endocrine-disrupting effects exist. Excessive intake or exposure during sensitive developmental periods may disrupt reproductive systems, alter pubertal timing, suppress thyroid function, or increase the risk of hormone-sensitive cancers. Individual differences in gut microbiome composition significantly influence phytoestrogen metabolism, resulting in substantial variation in biological responses among individuals. This review examines the primary dietary sources of phytoestrogens, elucidates their underlying mechanisms of action, and evaluates both their health benefits, potential adverse effects. This analysis identifies critical knowledge gaps and emphasises the importance of continued research to ensure safety and optimise phytoestrogen applications in nutritional interventions and functional food development

KEYWORDS

Phytoestrogens, Functional food, Endocrine Disruption, Isoflavones, Coumestans, Lignans, Stilbenes

1. INTRODUCTION

Phytoestrogens are plant-derived compounds that have gained significant attention for their ability to influence endocrine function by interacting with oestrogen receptors (ERs). Structurally, they resemble natural 17β-oestradiol and are mainly classified into two major groups: flavonoids and non-flavonoids. While flavonoids include isoflavones and coumestans, non-flavonoids consist of lignans and resorcinol derivatives, each with different distributions and biological potencies (Nikolić et al., 2017; Canivenc-Lavier and Bennetau-Pelissero, 2023). Isoflavones, predominantly found in soy products, are the most extensively studied due to their high affinity for binding to oestrogen receptors, especially ERβ, which is linked to bone, cardiovascular, and neurological health (Popa and Rusu, 2017). Coumestans, although less common, are present in sprouted legumes and alfalfa and exhibit even stronger oestrogenic activity than isoflavones (Patra et al., 2023). Lignans are found in flaxseeds and whole grains and are metabolised into enterolignans by gut microbiota (Patra et al., 2023). Resorcinol derivatives, such as resveratrol, are widespread in liverworts, higher plants, and peanuts (Nikolić et al., 2017). Due to their widespread presence in the diet and hormonal activity, phytoestrogens have been proposed as natural alternatives for managing endocrine-related conditions such as menopausal symptoms, osteoporosis, cardiovascular diseases, and metabolic disorders. However, their effects are complex, as they can act as both oestrogen agonists and antagonists, potentially leading to beneficial or disruptive endocrine outcomes.

The capacity of phytoestrogens to bind estrogen receptors and influence hormonal regulation depends on multiple factors, including their concentration, the distribution of receptors across different tissues, endogenous estrogen levels, and metabolic processing. Functioning as selective estrogen receptor modulators (SERMs), phytoestrogens exhibit estrogenic activity in conditions of estrogen deficiency, such as postmenopause, while demonstrating anti-estrogenic effects when endogenous estrogen is abundant (Intharuksa et al., 2025; Omeye, 2025). This dual function has positioned phytoestrogens as promising candidates in the exploration of alternatives to conventional hormone replacement therapy (HRT). For instance, empirical evidences indicate that soy isoflavones can alleviate menopausal symptoms, notably by reducing the intensity and frequency of hot flashes, enhancing bone mineral density, and promoting cardiovascular health through favourable modulation of lipid profiles and endothelial function (Shanmugaloga and Shilpa, 2024; Intharuksa et al., 2025). Furthermore, lignans have been associated with improved metabolic outcomes and a lowered risk of breast cancer, potentially attributable to their role in modulating estrogen metabolism and diminishing circulating estrogen concentrations (Omeye, 2025). Collectively, these findings underscore the therapeutic potential of phytoestrogens as a natural and accessible functional food for maintaining hormonal balance and supporting overall health.

Although phytoestrogens are associated with various health benefits, their potential endocrine-disrupting effects have raised significant concerns, particularly among individuals with hormone-sensitive conditions. Studies suggest that excessive exposure, especially during vulnerable developmental windows such as fetal life, infancy, and puberty, may impair reproductive function and contribute to long-term hormonal imbalances (Canivenc-Lavier and Bennetau-Pelissero, 2023; Byaruhanga,

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2025). For example, the effects of neonatal exposure to genistein (Wu et al., 2019). The results of subcutaneous injection of 100 mg/kg daily for 10 days in mice included disrupted ovarian activity and altered uterine morphology. Similarly, Isoflavones have also been reported to interfere with thyroid peroxidase activity, an enzyme essential for the iodination of tyrosine residues and the subsequent synthesis of thyroid hormones. By inhibiting this catalytic step, Isoflavones may impair thyroid hormone production, a risk that becomes more significant in individuals with insufficient iodine intake, thereby increasing their susceptibility to thyroid dysfunction (Bashar and Begam, 2020). Collectively, these findings underscore the complex nature of phytoestrogen activity and highlight the need for cautious evaluation of their safety in susceptible populations.

Given the widespread consumption of phytoestrogen-rich foods and their increasing use in dietary supplements, a thorough understanding of their endocrine-modulating effects is essential. The variability in individual responses, influenced by gut microbiota composition and overall hormonal status, further complicates their risk-benefit profile (Kumari et al. 2024; Serrano-López et al., 2025). Therefore, this review aims to provide an in-depth analysis of the mechanisms by which phytoestrogens influence endocrine function, highlighting both their health benefits and potential endocrine-disrupting risks. By synthesising current research on their benefits and adverse effects, this paper seeks to highlight existing knowledge gaps. It proposes directions for future research to enhance our understanding of phytoestrogens as both functional foods and endocrine disruptors.

2. Types And Sources Of Phytoestrogens

Phytoestrogens are primarily classified into four major classes: isoflavones, Lignans, Coumestans, and the emerging Stilbenes (Table 1).

Table 1: Major classes of Phytoestrogens and their hormonal modulation

Phytoestrogen Class	Compounds	Hormonal modulation
Isoflavones	Genistein, Daidzein, Glycitein	Bind to estrogen receptors (preferentially ERβ)
Lignans	Enterolactone, Enterodiol	Converted by gut microbiota into enterolignans with estrogenic activity
Coumestans	Coumestrol	Binding to ERs with strong estrogenic activity
Stilbenes	Resveratrol, Pterostilbene and piceatannol	Exhibits selective estrogen receptor modulation (SERM-like behaviour)

2.1 Isoflavones

Isoflavones are the most widely studied phytoestrogens because of their structural similarity to 17β-estradiol and their relatively high affinity for oestrogen receptors, particularly ER-β (Kim, 2021). The main isoflavones include genistein, daidzein, glycitein, and biochanin A. These compounds are primarily found in legumes, especially soybeans (Glycine max), and their products such as tofu and soy milk (Soyata et al., 2021; Kim, 2021). In their natural state, isoflavones exist as glycosides, which require hydrolysis, often facilitated by gut microbiota, to become biologically active (Huang et al., 2022; Nurmilah et al., 2024). Of particular interest is the microbial metabolite equol, derived from daidzein, which exhibits higher oestrogenic activity than its precursor. However, only 30–50% of individuals (depending on geography and diet) possess the bacteria necessary to produce equol efficiently (Leonard et al., 2022).

Geographical and cultural dietary patterns greatly influence isoflavone exposure. For example, Asian diets rich in fermented soy result in higher average isoflavone intake (25–50 mg/day) compared to Western diets (<1 mg/day) (Xie et al., 2013). This variation in exposure has been linked to epidemiological differences in hormone-dependent diseases, such as breast and prostate cancer (Nurmilah et al., 2024). However, concerns remain about potential hormonal disruption, especially in infants consuming soy-based formulas and in populations with high cumulative intake from supplements (Yeşildemir and Akdevelioğlu, 2021).

2.2 Lignans

Lignans are naturally occurring polyphenolic compounds that are predominantly present in plant-based foods, including seeds, whole grains, legumes, fruits, and vegetables. They are categorised as phytoestrogens because, after microbial metabolism in the gut, they are transformed into mammalian lignans like enterolactone and enterodiol (Laveriano-Santos et al., 2025). These metabolites share structural similarity with estrogens and are capable of interacting with estrogen receptors. This estrogen modulating ability has led to their growing use in functional foods, nutraceuticals, and dietary supplements. Beyond hormonal activity, lignans exhibit diverse biological effects, including antioxidant, anti-inflammatory, and anti-proliferative actions (Plaha et al., 2022; Sangiorgio et al., 2023). Their antioxidant function is attributed to their phenolic nature, which enables them to neutralise free radicals and reduce oxidative stress, a key factor in chronic illnesses, such as cardiovascular disorders and cancer (Plaha et al., 2022). Furthermore, lignans have been reported to inhibit enzymes such as aromatase and 5α-reductase, which play roles in steroid hormone metabolism, thereby aiding in the regulation of hormone-dependent conditions (Chen et al., 2021).

Flaxseed-enriched products such as flax bread, cereals, protein powders, and oilseed blends have gained considerable popularity in health-focused markets throughout Europe and Asia (Goyal et al., 2014). This rise in popularity is driven by epidemiological studies and clinical trials indicating that dietary flaxseed or isolated lignans can lower serum cholesterol, influence estrogen metabolism, and reduce markers of inflammation (Kauser et al., 2024). Importantly, enterolactone levels have been inversely linked to breast and prostate cancer risk, metabolic syndrome, and cardiovascular mortality, although establishing causality is still under investigation (Micek et al., 2021; Li et al., 2022).

2.3 Coumestans

Coumestans, especially coumestrol, are powerful phytoestrogens found in sprouted legumes, notably in alfalfa, clover (particularly subterranean clover), soybean sprouts, and mung bean sprouts (Canivenc-Lavier and Bennetau-Pelissero 2023; Verma et al., 2024). These sources tend to accumulate coumestans mainly during sprouting, especially under stress conditions such as fungal infection or extended storage (Tucak et al., 2020). While coumestans are relatively scarce in the modern processed Western diet, they can make a significant contribution to overall phytoestrogen intake in vegetarian and vegan diets, sprout-based foods, or through the use of herbal teas, tonics, and traditional preparations derived from sprouted legumes or forage crops.

In agricultural and veterinary contexts, coumestans have long been recognised for their deleterious effects on livestock reproduction. The most notable case is "clover disease", which has been described in sheep grazing on subterranean clover pastures. High coumestrol levels in these pastures were linked to anestrus, infertility, cervical hypertrophy, and altered oestrous cycles, leading to severe reproductive losses (Reed, 2016). Such findings underscore the potential impact of plant-derived estrogenic compounds on mammalian fertility, not only in domesticated animals but possibly in wildlife and humans exposed to concentrated sources.

2.4 Stilbenes

Stilbenes are a small but biologically versatile class of polyphenolic compounds characterised by a 1,2-diphenylethylene backbone. While they are less abundant in the human diet compared to isoflavones or lignans, stilbenes have gained substantial scientific interest due to their diverse bioactivities. The most extensively studied stilbene is resveratrol (3,5,4′-trihydroxystilbene), which naturally occurs in a limited number of dietary sources. These include the skins of grapes, particularly red grapes, as well as red wine, peanuts, berries, and certain traditional medicinal plants like Polygonum cuspidatum (El Khawand et al., 2018). Resveratrol is synthesised by plants as a defensive phytoalexin in response to stress factors such as UV light, fungal attack, or physical injury, which accounts for its varying levels among plant species and cultivars (El Khawand et al., 2018; Valletta et al., 2021).

Beyond resveratrol, other naturally occurring stilbenes such as pterostilbene and piceatannol are found in blueberries, grapes, passion fruit, and white tea (Remsberg et al., 2008). Pterostilbene, a dimethylated analogue of resveratrol, has greater lipophilicity and membrane permeability, which makes it more bioavailable and metabolically stable. It has shown antioxidant, anti-inflammatory, and ER-modulating effects both in vitro and in vivo, indicating that its biological effectiveness might be greater than that of resveratrol in certain contexts (Tian et al., 2023). Piceatannol, a hydroxylated metabolite of resveratrol, also interacts with oestrogen receptors and has demonstrated anticancer effects in cell

models, though it remains less understood in human studies (Horgan et al., 2019).

2.5 Dietary Sources of Phytoestrogens

Phytoestrogens are naturally occurring plant-derived compounds widely distributed in the human diet, especially in plant-based foods (Table 2). They are widely present in plant-based foods, with soybeans and soy products being the richest source of isoflavones (Domínguez-López et al., 2020; Verma et al., 2024). Flaxseeds and sesame seeds are the most concentrated sources of lignans, making a significant contribution to dietary intake (Domínguez-López et al., 2020). Other sources include legumes, which provide isoflavones and coumestans, as well as whole grains, nuts, seeds, and various fruits and vegetables, which offer smaller amounts but cumulatively increase overall exposure (Stark and Madar, 2002). Beverages such as red wine and green tea provide stilbenes and other polyphenolic phytoestrogens, further diversifying sources of intake (Verma et al., 2024).

Table 2: Dietary Sources of Phytoestrogens

Phytoestrogen Class	Compounds	Dietary Sources	Reference
Isoflavones	Genistein, Daidzein, Glycitein,	Soybeans, soy milk, tofu, tempeh, miso,	Domínguez-López et al., (2020); Verma et al., 2024)
Lignans	Enterolactone, Enterodiol	Flaxseed, sesame seeds	Domínguez-López et al., (2020)
Coumestans	Coumestrol	Alfalfa sprouts, clover sprouts,	Majumder et al., (2025)
Stilbenes	Resveratrol, pterostilbene and piceatannol	Red grapes, berries, red wine,	Remsberg et al., (2008)

Dietary exposure to phytoestrogens is influenced not only by the specific food sources consumed but also by broader cultural dietary patterns, agricultural practices, and post-harvest processing techniques (Thompson et al., 2006). Among these, food processing plays a pivotal role in determining both the concentration and bioavailability of phytoestrogens. Fermentation enhances bioavailability by hydrolysing glycosylated phytoestrogens into their more absorbable aglycone forms, whereas thermal treatments may lead to degradation or structural isomerisation of these compounds (Adam-Dima et al., 2024). For instance, fermented soy derivatives such as tempeh and miso exhibit elevated levels of bioactive isoflavones compared to unprocessed soybeans. In contrast, heat-sensitive phytoestrogens such as coumestrol and stilbenes are susceptible to degradation during thermal processing (Nurmilah et al., 2024). Consequently, food preparation methods should be considered when evaluating exposure or designing functional foods.

In addition to dietary sources, herbal products and nutraceuticals have become important contributors to phytoestrogen exposure in modern populations. A variety of botanicals used in traditional medicine, dietary supplements, and functional foods are rich in bioactive compounds with estrogenic activity. For example, red clover (Trifolium pratense) is particularly high in formononetin and biochanin A, two isoflavones known for their ability to modulate estrogen receptor signalling (Majumder et al., 2025). Similarly, Humulus lupulus (hops) is a significant source of prenylnaringenin, regarded as one of the most potent naturally occurring phytoestrogens (Shanmugaloga and Shilpa, 2024). Additionally, Glycyrrhiza glabra (liquorice root) provides glabridin, a flavonoid with both estrogenic and anti-estrogenic properties, contributing to its complex pharmacological effects (Intharuksa et al., 2025).

These herbal sources are widely marketed in the form of teas, capsules, and extracts for promoting hormonal balance, alleviating menopausal symptoms, and supporting bone and cardiovascular health. In many cultures, they also carry a long history of traditional use, which has reinforced consumer trust in their safety and efficacy. However, their high phytoestrogen potency raises critical questions about unintended endocrine consequences, particularly with long-term consumption. Studies have reported that concentrated extracts may elicit physiological effects comparable to synthetic estrogens, influencing reproductive function, thyroid activity, and metabolic regulation (Adam-Dima et al., 2024).

Furthermore, unlike dietary phytoestrogens obtained through regular food consumption, nutraceutical formulations often deliver phytoestrogens in concentrated amounts, potentially surpassing levels usually found in a natural diet (Patisaul, 2016). This raises the risk of endocrine disruption and individual responses that vary depending on gut microbiota composition and hormonal status (Szukiewicz, 2023; Byaruhanga, 2025). Therefore, although herbal phytoestrogens present promising options for therapeutic interventions, they also underscore the importance of rigorous clinical assessment and regulatory oversight to balance their health benefits against potential risks (Szukiewicz, 2023; Byaruhanga, 2025).

2.6 Environmental sources of phytoestrogens

Environmental exposure to phytoestrogens is an increasingly concerning issue. Discharges from food processing facilities, livestock operations, and municipal wastewater have been shown to release measurable levels of isoflavones and lignans into aquatic environments (Kolpin et al., 2002; Czarny et al., 2017). These compounds have been detected in surface waters, agricultural runoff, and municipal wastewater, where they may impact aquatic organisms by mimicking natural hormones (Kolpin et al., 2002; Guimarães et al., 2024). Chronic exposure studies have shown that genistein and daidzein, two common phytoestrogens, can exert toxic effects on marine invertebrates, with toxicity levels comparable to synthetic estrogens such as estradiol valerate (Guimarães et al., 2024). The unintended release of phytoestrogens from food processing industries and livestock operations presents ecological risks and may complicate the assessment of synthetic endocrine disruptors in environmental monitoring efforts (Czarny et al., 2017). Furthermore, phytoestrogens in aquaculture feed have been demonstrated to interfere with fish reproduction and sex differentiation, raising concerns about their broader ecological impact (Badamasi et al., 2020; Farooq et al., 2025). Such contamination can produce estrogenic effects on aquatic wildlife, complicating the risk assessment of human-made endocrine disruptors (Guimarães et al., 2024). Therefore, phytoestrogens should be regarded not only as dietary components but also as environmental pollutants, requiring ecotoxicological monitoring and regulatory scrutiny, particularly in developing regions where wastewater treatment infrastructure may be lacking (Badamasi et al., 2020).

3. Mechanisms Of Endocrine Modulation

Phytoestrogens exhibit structural similarity to 17β-estradiol, allowing them to interact with various components of the endocrine system. Their actions may be estrogenic, anti-estrogenic, or modulatory, depending on concentration, receptor subtype distribution, and physiological context. The key mechanisms of endocrine modulation include estrogen receptor binding, enzyme regulation and hormone-binding protein modulation, and metabolic transformation mediated by gut microbiota (Figure 1).

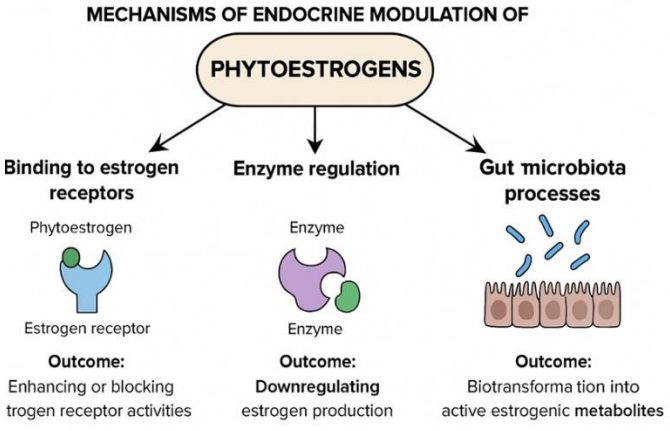

Figure 1: Mechanisms of endocrine modulation by phytoestrogens

3.1 Binding to estrogen receptors

Phytoestrogens, a broad group of plant-derived polyphenolic compounds, mainly exert their biological effects through interactions with estrogen receptors (ERs), which are divided into two main subtypes: ERα and Erβ. These receptors, encoded by separate genes and showing different tissue distribution, regulate a wide range of estrogenic responses. ERα is mainly found in reproductive tissues such as the uterus and mammary glands, while ERβ is more common in the bone, brain, cardiovascular system, and prostate (Lecomte et al., 2017). Phytoestrogens act as selective estrogen receptor modulators (SERMs), functioning as agonists or antagonists

depending on the receptor subtype, tissue environment, and levels of circulating endogenous estrogens (Sirotkin and Harrath, 2014).

Among the major classes of phytoestrogens, isoflavones, particularly genistein and daidzein, exhibit a higher binding affinity for Erβ. This receptor selectivity underpins their potential roles in promoting bone health, enhancing neuroprotective mechanisms, and supporting cardioprotective and metabolic regulation (Vitale et al., 2013; Omeye, 2025). Genistein, for instance, activates ERβ-mediated transcriptional pathways that inhibit osteoclastic activity and stimulate osteoblastic differentiation, contributing to bone health in postmenopausal individuals (Omeye, 2025). In contrast, lignans abundant in flaxseeds and coumestans found in legumes such as alfalfa undergo distinct metabolic transformations and exhibit unique receptor interactions. Lignans are converted by intestinal microbiota into enterolignans (enterodiol and enterolactone), which possess moderate estrogenic activity and may influence hormone-sensitive tissues such as the breast and prostate (Sangiorgio et al., 2023; Krishna et al., 2022; Laveriano-Santos et al., 2025). Coumestrol, the principal coumestan, demonstrates high affinity for both ERα and ERβ and has been implicated in modulating cellular proliferation and apoptosis in estrogen-responsive cancers (Krishna et al., 2022).

3.2 Enzyme regulation

Phytoestrogens can influence hormonal balance through various biochemical pathways, mainly enzyme regulation and hormone-binding protein modulation. One of the most researched mechanisms involves their ability to inhibit aromatase (CYP19A1), the key enzyme responsible for converting androgens such as testosterone and androstenedione into estrogens. By decreasing aromatase activity, phytoestrogens, particularly flavonoids like chrysin, naringenin, and genistein, can lower endogenous estrogen synthesis, a process that has attracted considerable attention in the context of estrogen-sensitive cancers such as breast and endometrial cancers (Lephart, 2015). In these cases, reducing estrogen availability may slow tumour growth and progression. Furthermore, in postmenopausal women, where estrogen production shifts from the ovaries to peripheral sources, aromatase inhibition by dietary phytoestrogens may help reduce risks linked to unopposed estrogen exposure, including endometrial hyperplasia and hormone-dependent tumour development (Hajirahimkhan et al., 2023).

Apart from enzymatic control, phytoestrogens also influence the bioavailability of circulating sex hormones through their effect on sex hormone-binding globulin (SHBG). Synthesised mainly in the liver, SHBG binds estrogens and androgens with high affinity, regulating the amount of free, biologically active hormones in the bloodstream. Some studies have shown that phytoestrogens, especially isoflavones and lignans, can increase hepatic SHBG expression, leading to lower levels of free estradiol and testosterone (Briansó-Llort et al., 2024; Abdel-latif et al., 2023). This regulation of hormone levels not only maintains endocrine balance but also interacts with broader metabolic processes. For example, higher SHBG levels have been linked to better insulin sensitivity, more favourable lipid profiles, and increased bone mineral density, suggesting that phytoestrogens might help protect against metabolic syndrome, osteoporosis, and cardiovascular disease (Zhang et al. 2024).

3.3 Gut microbiota processes

The estrogenic activity of phytoestrogens is not determined solely by their dietary intake but rather by their metabolic transformation, largely mediated by gut microbiota. Once consumed, phytoestrogens undergo deglycosylation and other biotransformations that influence their bioavailability and receptor-binding capacity (Farhat et al., 2023). For example, the isoflavone daidzein, abundant in soy and soy-based products, can be converted by intestinal bacteria into equol, a metabolite with significantly greater affinity for oestrogen receptor beta (ERβ) (Lv et al., 2024; Sekikawa et al., 2022). However, only 30–50% of individuals carry the necessary microbial strains, leading to notable interindividual variation in physiological responses to isoflavone-rich diets (Alotaibi et al., 2021). This “equol-producer” phenotype has been linked to improved relief from menopausal symptoms, bone protection, and reduced cardiovascular risk (Uchiyama, 2024).

Similarly, lignans present in flaxseed, sesame, and whole grains are metabolised into enterolignans such as enterodiol and enterolactone, which function as weak agonists of oestrogen receptors. Although their potency is lower than that of equol, enterolignans provide several health benefits, including anti-inflammatory effects, regulation of lipid metabolism, and potential protective roles against hormone-dependent cancers (Canivenc-Lavier and Bennetau-Pelissero, 2023).

Coumestans, particularly coumestrol from clover and alfalfa sprouts, undergo microbial conversion into highly active estrogenic derivatives that can bind both ERα and ERβ, providing antioxidant and bone-protective benefits, although excessive intake raises concern of endocrine disruption (Park et al., 2023; Krishna et al., 2022). Stilbenes such as resveratrol, found in grapes, red wine, and peanuts, are metabolised into bioactive compounds with both estrogenic and potent antioxidant properties, contributing to cardiovascular and neuroprotective effects (Renke et al., 2025; Wu et al., 2025).

4. Health Benefits Of Phytoestrogens

The potential health benefits of phytoestrogens are widely documented, particularly in conditions related to estrogen deficiency or dysregulation (Figure 2). One of the most extensively studied applications is in menopausal symptom management, where soy isoflavones alleviate vasomotor symptoms such as hot flashes and night sweats by binding to estrogen receptor beta (ERβ) in the hypothalamic thermoregulatory centre. This provides mild estrogenic stimulation, helping to stabilise temperature regulation and offering a natural alternative to hormone replacement therapy (HRT) (Luan et al., 2025; Chen and Chen, 2021). Furthermore, phytoestrogens play a crucial role in bone health, not only by reducing osteoclastic activity but also by enhancing osteoblast differentiation, which helps maintain bone health and lowers the risk of osteoporosis in postmenopausal women (Jayusman et al., 2023).

Alongside menopausal health, phytoestrogens demonstrate cardioprotective effects by enhancing endothelial function, lowering low-density lipoprotein (LDL) cholesterol, and exhibiting anti-inflammatory effects. Notably, isoflavones enhance endothelial nitric oxide synthase (eNOS) activity, leading to vasodilation and increased arterial flexibility, which may help reduce the risk of cardiovascular disease (CVD) (Gulati et al., 2025). Furthermore, phytoestrogens inhibit lipid peroxidation and decrease pro-inflammatory cytokines, adding an extra advantage of vascular protection (El Omari et al., 2024).

Beyond cardiovascular health, phytoestrogens provide neuroprotective effects, with evidence indicating a potential role in reducing the risk of cognitive decline and neurodegenerative diseases such as Alzheimer’s disease. Genistein and daidzein have been shown to protect against β-amyloid plaque formation and oxidative stress, two key factors in Alzheimer’s disease pathology (Singh et al., 2024). Furthermore, their antioxidant and anti-inflammatory properties may help reduce inflammation and neuronal death, thereby further maintaining cognitive function in ageing populations (Gorzkiewicz et al., 2021).

Other endocrine-related benefits of phytoestrogens include their involvement in glucose metabolism and insulin sensitivity, making them relevant in the prevention and management of diabetes. Isoflavones influence peroxisome proliferator-activated receptors (PPARs), which control glucose uptake, lipid metabolism, and insulin signalling (Verma et al., 2024). Research suggests that regular intake of soy products can improve fasting glucose levels and insulin resistance, lowering the risk of type 2 diabetes mellitus (Huang et al., 2024).

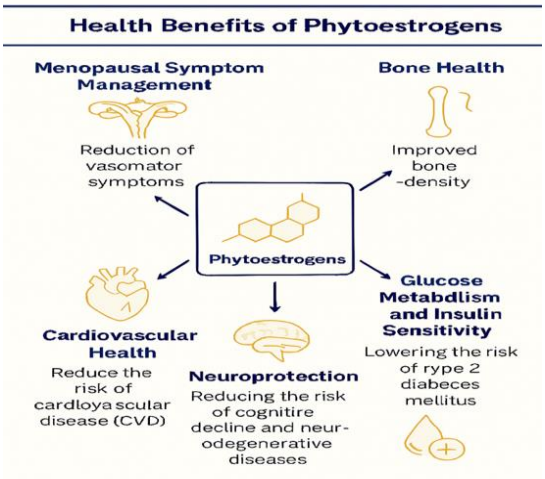

Figure 2: Health Benefits of Phytoestrogens

5. Potential Endocrine-Disrupting Effects Of Phytoestrogens

Despite their beneficial effects, phytoestrogens can also exert endocrine-disrupting effects, particularly when consumed in excessive amounts or in vulnerable populations (Figure 3). One of the main concerns is their potential to interfere with reproductive health, especially during critical

developmental windows such as fetal development, infancy, and puberty. Some studies suggest that high phytoestrogen intake during these periods may lead to altered reproductive function later in life (Krishna et al., 2022; Mohammed et al., 2024). For example, animal models have linked genistein exposure to disrupted ovarian follicle development, altered puberty onset, and fertility issues, possibly due to suppression of gonadotropin-releasing hormone (GnRH) pulsatility, which affects luteinizing hormone (LH) and follicle-stimulating hormone (FSH) regulation (Krishna et al., 2022).

Thyroid function disruption is another concern, as isoflavones have been shown to inhibit thyroid peroxidase (TPO), an enzyme vital for thyroid hormone production. This may contribute to hypothyroidism, especially in individuals with iodine deficiency, where lowered thyroxine (T4) and triiodothyronine (T3) levels lead to compensatory increases in thyroid-stimulating hormone (TSH) (Otun et al., 2019; Sathyapalan et al., 2018). Clinical studies have expressed concern about soy-based infant formulas, which have been linked to higher TSH levels in newborns, indicating that early exposure may interfere with normal thyroid function (Lv et al., 2024).

Furthermore, there is ongoing debate about the safety of phytoestrogen consumption in individuals with hormone-sensitive cancers, such as breast and prostate cancer. While some studies indicate that phytoestrogens may have protective effects by competing with endogenous estrogens and primarily activating estrogen receptor beta (ERβ), which possesses anti-proliferative properties, others express concerns that high phytoestrogen intake could promote tumour growth in ERα-dominant breast cancer subtypes (Torrens-Mas and Roca, 2020; Dharshini et al., 2023; Manoharan et al., 2025). This dual behaviour highlights the complexity of phytoestrogen-cancer interactions and suggests that personalised dietary advice may be necessary for populations at high risk of estrogen-driven cancers (Manoharan et al., 2025).

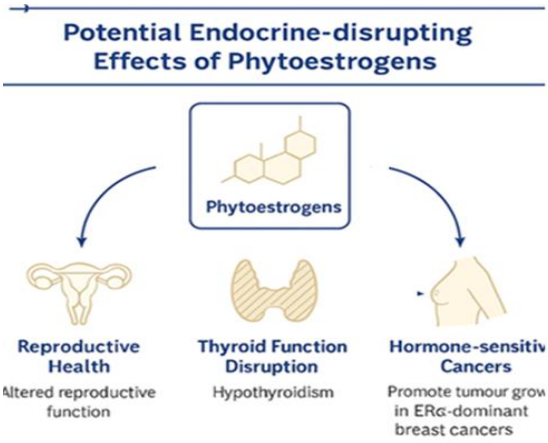

Figure 3: Potential endocrine-disrupting effects of phytoestrogens

6. Knowledge Gaps And Future Research Directions

Despite extensive research on phytoestrogens, significant gaps remain in our understanding of their dual roles as functional food and endocrine disruptors. First, the bioavailability and metabolism of phytoestrogens remain poorly understood, as individual variation driven by gut microbiota composition and dietary patterns considerably influences their biological activity. Second, current research often focuses on isolated compounds, such as genistein or daidzein, while the synergistic or antagonistic interactions among multiple phytoestrogens present in whole foods are largely unexamined. Third, the long-term endocrine and epigenetic effects of exposure during key developmental periods such as pregnancy, puberty, and menopause remain poorly understood, emphasising a lack of clarity across various life stages. Lastly, the distinction between beneficial modulation and adverse disruption remains ambiguous, particularly in the context of chronic, low-dose exposure from dietary sources versus supplements, making accurate risk assessment challenging.

To improve our understanding, future research should focus on well-designed, long-term studies involving diverse demographic groups to determine dose-response relationships, efficacy, and safety of phytoestrogens as functional foods. Combining metabolomics and gut microbiome profiling can help clarify individual differences in bioavailability and bioactivity, enabling personalised dietary or therapeutic advice. Research should also examine the effects of whole foods and dietary patterns, rather than isolated compounds, to reflect real-world exposure and possible synergistic effects. Moreover, studies should explore epigenetic and transgenerational impacts, particularly regarding developmental exposures and their potential to affect endocrine function or disease risk later in life. Advanced toxicological modelling and systems biology approaches can aid in establishing thresholds that differentiate endocrine modulation from disruption, guiding regulations for functional foods and nutraceuticals containing phytoestrogens. Lastly, interdisciplinary collaboration among nutritionists, endocrinologists, toxicologists, and policymakers will be vital to turn scientific insights into evidence-based guidelines that maximise health benefits while minimising risks.

7. Conclusion

Phytoestrogens are bioactive plant compounds that can influence endocrine function through various mechanisms. They hold potential for treating menopausal symptoms, preserving bone density, enhancing cardiovascular health, and supporting metabolic regulation. However, concerns remain about their endocrine-disrupting effects, particularly regarding reproductive health, thyroid function, and hormone-sensitive cancers. The biological impact of phytoestrogens largely depends on the dose, timing of exposure, and individual metabolic differences. While moderate consumption may confer health benefits, excessive intake or exposure during sensitive developmental periods, such as fetal development and infancy, could lead to adverse effects. Variations between individuals, influenced by gut microbiota composition, add further complexity to their hormonal actions. To ensure their safe use, more comprehensive clinical trials are necessary to determine appropriate dosage guidelines, assess responses across diverse populations, and better understand their therapeutic potential. Therefore, a balanced, evidence-based approach that considers both benefits and health risks is essential for the effective integration of phytoestrogens into nutrition and functional food strategies.

Competing Interests

"The author declares no conflict of interest."

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Ethical Approval

This is a review paper; no animals were involved in the study, therefore, no approval from the research ethics committee was required.

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