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Phytoestrogens: Unlocking the Power of Plant Based Estrogens

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ABSTRACT

Phytoestrogens, naturally occurring plant compounds with estrogen-like activity, have garnered significant attention for their potential health benefits in both males and females. These compounds, found in a variety of foods such as soybeans, flaxseeds, and whole grains, mimic the action of estrogen in the body by binding to estrogen receptors. In females, phytoestrogens have been particularly noted for their role in alleviating menopausal symptoms. They can help reduce hot flashes, night sweats, and vaginal dryness, offering a natural alternative to hormone replacement therapy (HRT). Furthermore, phytoestrogens have been linked to a reduced risk of osteoporosis by promoting bone health and improving bone density, crucial for postmenopausal women. Males also benefit significantly from phytoestrogens. Studies suggest that these compounds can help maintain prostate health and reduce the risk of prostate cancer by inhibiting the growth of cancer cells. Additionally, phytoestrogens have been associated with improved cardiovascular health in both genders. They contribute to lowering cholesterol levels and improving arterial function, thereby reducing the risk of heart disease. Beyond these benefits, phytoestrogens possess potent antioxidant and anti-inflammatory properties, enhancing overall immune function and potentially offering protective effects against certain chronic diseases such as diabetes and obesity. Their ability to modulate hormone levels without significant side effects makes them a promising component of a balanced diet for long-term health maintenance. This study attempts to compile foods high in phytoestrogens and herbs used in Ayurvedic medicine with its super benefits.

Key words: *Phytoestrogens, Ayurvedic herbs, phytoestrogen diet, natural estrogens*

INTRODUCTION

Estrogens: Estrogens are a group of steroid sex hormones found both in males and females, that play a crucial role in the development and maintenance of reproductive organs and secondary sex characteristics.^[1,2]

Estrogen predominantly present in females than males, their levels fluctuate throughout a woman's life, rising during puberty, peaking during the reproductive years, and declining during menopause. Consistently high or low levels of estrogen may indicate an underlying health condition.^[2,3]

Estrogens are also used as medications, such as in menopausal hormone therapy to alleviate symptoms of menopause and in hormonal birth control to prevent pregnancy. However, hormone therapy may increase the risk of certain medical problems, such as blood clots and breast cancer. In addition to their natural occurrence, estrogens can also be found in the environment as xenoestrogens, which are synthetic compounds that mimic the effects of estrogens and can potentially disrupt the endocrine system, while phytoestrogens, which are naturally occurring substances, help the body function better when estrogen deficiency occurs.

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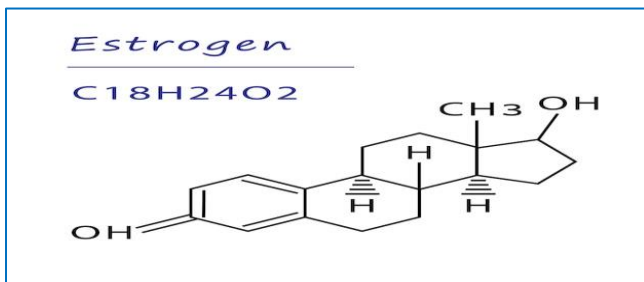


Fig. 1: Structure of Estrogen

Types

There are four main types of estrogen.^[2,3]

- **Estrone (E1):** This is the primary type of estrogen in males. It is also the primary form of estrogen in females after menopause. The ovaries, placenta, testicles, and fat tissue produce estrone from androstenedione or androgens.
- **Estradiol (E2):** This is the most potent form of estrogen, and its concentration is highest in females of childbearing age. Doctors use this form of estrogen as a marker for ovary health.
- **Estriol (E3):** The placenta produces this type of estrogen, which reaches peak levels during pregnancy. The amount of estriol increases as the fetus grows.
- **Estetrol:** produced only during pregnancy

Sources

- **Estrogens:** Produced in the ovaries primarily in women, for men in testes, with small amounts from the adrenal glands and fat tissue.^[1]

Importance of Estrogens:^[3,4,5,6]

Estrogens are a group of hormones that play a crucial role in various physiological processes in the body. Here are the benefits of estrogens and their actions in detail:

A. Reproductive Health

- **Puberty and Sexual Development:** Estrogens are responsible for the development of secondary sex characteristics, such as breast growth, pubic hair, and axillary hair, during puberty

- **Menstrual Cycle Regulation:** Estrogens regulate the menstrual cycle, ensuring regular ovulation and menstruation.
- **Fetal Development:** Estrogens support fetal development during pregnancy, particularly in the first trimester. Also, maintains the health of the placenta during pregnancy
- **Menopause:** Estrogens help regulate the transition into menopause, reducing the risk of osteoporosis and cardiovascular disease
- **Vaginal Health:** Estrogens maintain vaginal health by promoting the growth of vaginal tissue and maintaining the pH balance of the vagina.

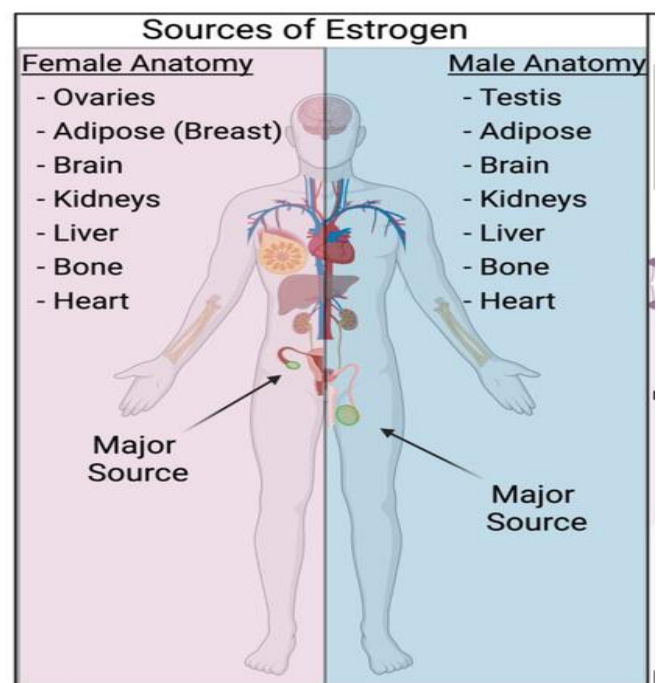


Fig. 2: Estrogen Synthesis in Body

In males

- **Modulation of Libido and Erectile Function:** Estradiol helps regulate libido and erectile function in men. It is essential for maintaining normal sexual function and performance.
- **Spermatogenesis:** Estrogens, particularly estradiol, modulate spermatogenesis at multiple levels, including the hypothalamus-pituitary-gonadal axis, Leydig cells, Sertoli cells, and germ cells. This

regulation is both inhibitory and stimulatory, indicating a complex balance.

- Estradiol synthesis is increased in areas related to sexual arousal in the brain, indicating its involvement in sexual behaviour and arousal.
- Penile Function: Estrogen receptors are found throughout the corpus cavernosum, particularly around neurovascular bundles, which suggests a role in maintaining penile function and blood flow.
- Local Production: In males, estradiol is produced locally by Leydig and Sertoli cells in the testes, as well as through aromatization of testosterone in peripheral organs.
- Role in Brain Development: Local production of estradiol in the male cerebellum is important for vestibular-ocular reflex adaptation.

B. Bone Health

- Bone Density: Estrogens help maintain bone density, reducing the risk of osteoporosis and fractures.
- Bone Strength: Estrogens promote bone strength by regulating calcium and vitamin D levels.

C. Cardiovascular Health

- Blood Pressure Regulation: Estrogens help regulate blood pressure, reducing the risk of cardiovascular disease.
- Cholesterol Levels: Estrogens lower cholesterol levels, reducing the risk of cardiovascular disease.

D. Brain Health

- Neuroprotection: Estrogens have neuroprotective effects, reducing the risk of neurodegenerative diseases such as Alzheimer's and Parkinson's.
- Memory and Learning: Estrogens improve memory and learning by promoting the growth of new neurons and neural connections.

E. Skin and Hair Health

- Skin Health: Estrogens promote skin health by regulating collagen production and improving skin elasticity.
- Hair Growth: Estrogens promote hair growth by regulating the growth cycle of hair follicles.

F. Other Benefits

- Mood Regulation: Estrogens regulate mood, reducing the risk of depression and anxiety. Estrogen is positively associated with serotonin, which is a neurotransmitter that regulates mood. Estrogen receptors are present in various brain regions, including the amygdala, hippocampus, and prefrontal cortex, which are involved in mood regulation. Estrogen can modulate the activity of these regions, influencing mood and emotional processing.
- Immune System Regulation: Estrogens regulate the immune system, reducing the risk of autoimmune diseases.

Levels of Estrogen:^[7,8]

In women



	Estrone (E1)	Estradiol (E2)
Before puberty	Undetectable to 29 pg/ml	Undetectable to 20 pg/ml
During puberty	20 – 200 pg/ml	Undetectable to 350 pg/ml
Before menopause	17 – 200 pg/ml	15 – 350 pg/ml
After menopause	7 – 40 pg/ml	Less than 10 pg/ml

Signs and symptoms of high estrogen levels in women

In females, having too much estrogen may cause:

- weight gain, especially around the hips and waist
- Irregular menses
- worse PMS than usual
- fatigue
- fibroids in the uterus
- fibrocystic breast lumps
- low sex drive
- low mood or anxiety

Additional possible symptoms include:

- bloating
- headaches
- disrupted sleep
- hair loss

In men

	Estrone (E1)	Estradiol (E2)
Before puberty	Undetectable to 16 pg/ml	Undetectable to 13 pg/ml
During puberty	Undetectable to 60 pg/ml	Undetectable to 40 pg/ml
Age 18 years and over	10 – 60 pg/ml	10 – 40 pg/ml

Signs and symptoms of high estrogen levels in men

In males, having too much estrogen may cause:

- Gynecomastia
- Erectile Dysfunction
- Infertility
- Depression.

Complications of high estrogen levels

If a person has consistently high estrogen for an extended period, this increases their risk of:

- High blood pressure

- blood clots
- hypocalcemia,
- breast cancer
- cervical cancer
- High estrogen may also worsen pre-existing conditions, such as asthma or epilepsy.
- high levels of free estriol have an increased risk of gestational diabetes in pregnancy.

Low level of estrogen women:

The most common reason for low estrogen in women is menopause or surgical removal of the ovaries.

Symptoms of low estrogen include:

- Menstrual periods that are less frequent or that stop
- Hot flashes
- Trouble sleeping
- Vaginal dryness and thinning
- menstrual migraine

Men: Low estrogen in men can cause excess belly fat and low sexual desire

Synthesis of Estrogen:^[2]

Estrogens: Endogenous estrogen is produced and released directly into the bloodstream for systemic effects.

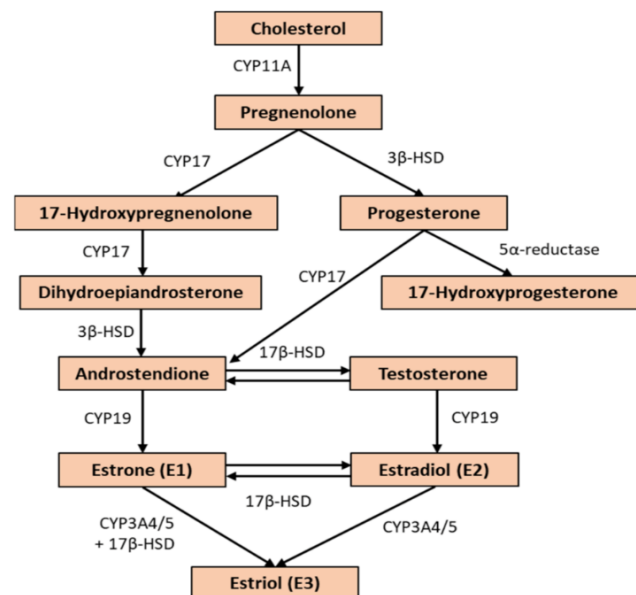


Fig. 3: mechanism of synthesis of estrogen

Table 1: Estrogen Receptors and Sites of Action^[9]

Estrogen Receptor	Sites of Action
ER- α	Uterus, breasts, bones, and hypothalamus
ER- β	Ovaries, prostate, lungs, and cardiovascular system

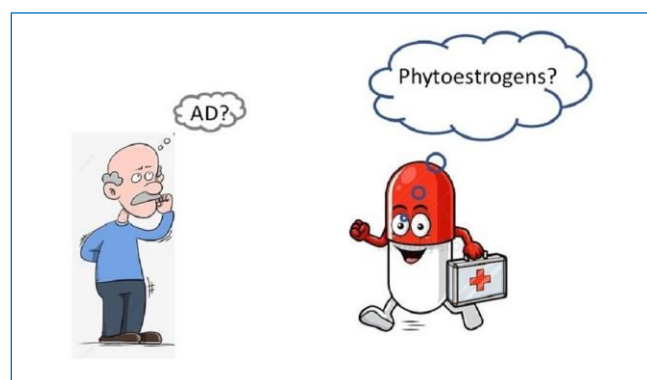
- **Estrogens:** Bind to estrogen receptors in various tissues to regulate gene expression and physiological functions.

Disadvantages:

- May cause side effects such as hot flashes and mood swings
- May increase the risk of certain cancers
- May interact with other medications.

Phytoestrogen

Phytoestrogens are plant-derived compounds that mimic estrogen's activity in the body. The structure of phytoestrogens is characterized by a close structural similarity to estrogens, allowing them to act as estrogenic factors and interfere with hormonal signaling.^{[8][9]} Phytoestrogens are naturally occurring compounds found in plants and are classified into different classes based on their chemical structure. The main classes of phytoestrogens include isoflavones, lignans, and stilbenes, can interact with estrogen receptors, mimicking estrogen's effects but with lower potency.



- Consumed through diet- plant-based sources, absorbed in the digestive system, and can exert estrogenic effects in the body.

- Can provide benefits like relief from hot flashes, potential cancer protection, and cardiovascular health support.
- Offer benefits like relief from menopausal symptoms and potential cancer protection but may interact with medications and have varying effects.^[10]

Types of Phytoestrogens

Based on the provided sources, the chemical structure of phytoestrogens is characterized by a phenolic ring and two hydroxyl groups, which are crucial for binding to estrogen receptors (ER).

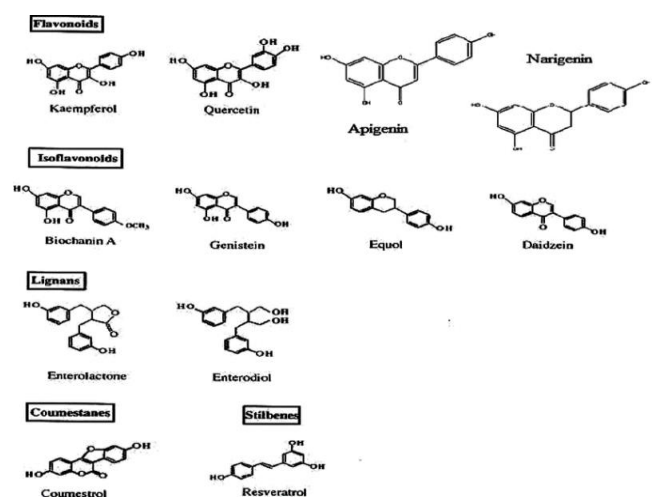
Phytoestrogens are classified into three main classes: Flavonoids, lignans, and stilbenes.

Flavonoids have a typical structure of C6-C3-C6, with two aromatic rings joined by a chain of 3 carbons cycled through an oxygen atom.

The subclasses of flavonoids include isoflavonoids (isoflavones and coumestans), flavones, flavonols, flavan-3-ols (catechins), flavanones, chalcones, and anthocyanins.

The chemical structure of phytoestrogens, is crucial for their interaction with estrogen receptors and their estrogenic or antiestrogenic effects (i.e.; amphoteric effects) in the body.

The structural similarity of phytoestrogens to human sex hormones allows them to bind to estrogen receptors and modulate hormonal responses, impacting various physiological processes.

**Fig. 4: structures of types of phytoestrogens**

Receptor Mechanism^[9]

Phytoestrogens can bind to estrogen receptors (ER- α and ER- β) and mimic or antagonize the effects of estrogen. The similarities in structure allow them to interact with estrogen receptors, but they are generally weaker than endogenous estrogen.

It is due to the chemical structure of phytoestrogens that they can interact with estrogen receptors and have either estrogenic or antiestrogenic (i.e., amphoteric) effects on the body.

Absorption and Metabolism^[11]

Daidzin, contained in soy products, is **hydrolyzed by the bacterial beta-glucosidase** generating aglycones (primary metabolites). In addition, the colonic microflora is capable of transforming aglycones into secondary metabolites and bacterial end-products that are eliminated with feces. Both primary and secondary metabolites undergo either **glucuronidation or sulfidation by intestinal epithelial cells** and hepatocytes. Once in the bloodstream, these conjugated products reach target tissues and later on are excreted in urine or bile. In the latter case, they can be absorbed again by the intestine (enterohepatic circulation) or are excreted in feces as bacterial end-products or unconjugated forms.

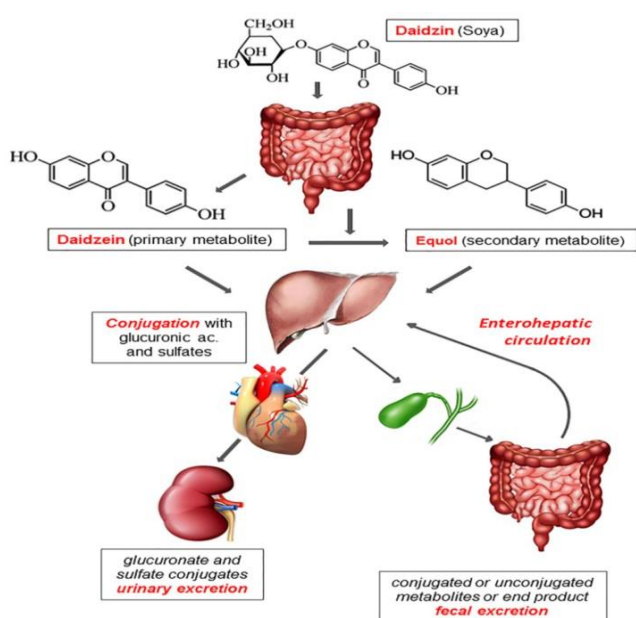


Fig. 5: absorption, metabolism and excretion of phytoestrogens

Phytoestrogen Intake Levels^[12,13]

Comparison of dietary isoflavone and lignan intakes in various countries.		
Countries	Isoflavones	Lignans
	(mg/day per person, expressed as mean \pm SD)	
Mediterranean countries ^[15] (Greece, Spain, Italy, and Southern France)	0.46 \pm 0.05	1.02 \pm 0.01
Non-Mediterranean European countries ^[15] (Northern France, Germany, the Netherlands, Denmark, Sweden, Norway)	0.76 \pm 0.03	1.26 \pm 0.01
United Kingdom ^[15]	2.34 \pm 0.16	1.60 \pm 0.04
China ^[16,17]	40.8 \pm 28.7 (in women)	n.d.
	36.2 \pm 24.4 (in men)	
Japan (range) ^[18,19]	20.8-46.2	n.d.

n.d.: not determined.

- Average daily intake in East and Southeast Asia is estimated at 20-50 mg
- Average intake in the United States is 0.15-3 mg per day
- Average intake in Europe is much lower at 0.49-0.66 mg per day

Functions of Phytoestrogens^[3]

- Mimic the effects of estrogen in the body
- May help relieve menopausal symptoms
- May help prevent osteoporosis
- May have anti-cancer properties
- May have anti-inflammatory properties
- Prevention and treatment of menopausal symptoms
- Controls aging of skin
- Prevents and controls osteoporosis
- Maintains cardiovascular health, regulates cholesterol levels
- supports immune system malfunction, metabolic disorders, and neurodegenerative diseases.

Disadvantages

- May interact with certain medications

- May not be suitable for all types of cancer
- Regulation and safety are not well-established
- Allergic reactions
- Gut disturbances – nausea, vomiting, diarrhoea
- Adversely affects fertility-increased phytoestrogen diet seem to reduce the occurrence of pregnancies and may decrease the sperm level in men
- Cause hormonal issues- early consumption could lead to hormonal imbalances later in life
- May stimulate breast carcinoma
- Increase the risk of endometrial CA, vaginal bleeding, endometrial hyperplasia,
- Suppress thyroid function
- Increase the risk of cognitive decline.

Note: side effects are more common in women older than 55 years.

Natural Sources of Phytoestrogens [13,14,15,16]



Food Source	Phytoestrogen Quantity (mg/100g)	Type of Phytoestrogen	Action
Vegetables			
Soybeans	103-153	Isoflavones	improves fertility, reduces menopausal symptoms (hot flashes, osteoporosis), supports bone health, heart

			health, and breast health
Alfalfa sprouts	0.5-1.5	Coumestans	
Mung bean sprouts	0.5-1.5	Isoflavones	
Yams	0.5-1.5	Isoflavones	
Legumes (Lentils, chickpeas)	0.5-1.5	Isoflavones	
carrot	0.5-1.5	Lignans	
Pinto beans	0.5-1.5	Lignans	Rich in nutrients and iron, reduce the risk of infertility
Garlic	0.5-1 mg/100g	Lignans	estrogenic effects, improves fertility, reduces menopausal symptoms (hot flashes, osteoporosis), supports bone health, reduces the risk of heart diseases.

Fruits

Pomegranate	0.5-1.5	Isoflavones	
Grapes(red variety)	0.2-1.5	Stilbenes	
Apple	0.5-1.5	Isoflavones	
Peaches	0.5-1.5	Isoflavones	Contains many essential nutrients, it may reduce the risk of heart diseases
Berries (blueberry, cranberry, strawberry)	0.5-1.5	Isoflavones	Lowers the risk of obesity and heart diseases

Nuts & Seeds

Flaxseeds	85-140	Lignans	Reduces the risk of cardiac diseases, has beneficial effects on fertility, reduces the breast tumour growth
Flaxseed Flour (Defatted)	11.7-24.1	Lignans	

Flaxseed Flour (Whole)	6.1-13.3	Lignans	
Sesame seeds	0.5-1.5	Lignans	Improves sperm count and motility, release of an egg, maintains bone health, lipid lowering activity
Sunflower seeds	0.5-1.5	Lignans, coumestans	
Almond	0.5-1.5	Isoflavones	
Walnuts	0.5 – 1.5	Isoflavones	Rich in omega 3 fatty acids, protein and nutrients. Reduces menopausal symptoms-osteoporosis, improves mood, reduces hotflashes
Peanuts	0.1 -1.2	Lignans	Relief from menopausal symptoms, supports bone health, heart health, reduces the risk of breast and prostate cancer, neurodegenerative diseases.
Dry Fruits			
Dried Fruits (e.g., Dates, Prunes, Dried Apricots)	0.5-1.5	Lignans	Good source of phytoestrogens and rich in fiber
Others			
Red Clover	12-15	Isoflavones	
Soy Protein Isolate (Powder)	91.05	Isoflavones	Manage hormonal imbalance and lowers the risk of breast cancer, heart disease and osteoporosis
Soy product (Natto)	82.29	Isoflavones	
Soy products (tofu, tempeh, miso)	20-91	isoflavones	
Coffee	0.5-1.5	Lignans	

Olive oil	0.5-1.5	Lignans	
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However, it's important to note that the research on phytoestrogens has been mixed, with some studies showing benefits and others finding no significant effects. The therapeutic effects may be influenced by individual factors like gut bacteria and ability to metabolize phytoestrogens

Note: The phytoestrogen quantities are approximate and may vary based on the specific food item, preparation method, and cooking process. This table provides a comprehensive overview of natural sources of estrogen and phytoestrogens, including their quantities and types.

Ayurvedic Medicines with Phytoestrogens [17,18,19,20,21]

Drugs	Botanical name	Effects
<i>Shatavari</i>	<i>Asparagus racemosus</i>	Reduces the severity of menopausal syndrome, enhances fertility, balances hormones
<i>Ashoka</i>	<i>Saraca asoca</i>	Effective in hormone imbalance
<i>Ashwagandha</i>	<i>Withania somnifera</i>	Help balance hormone levels control stress, boost libido and sexual function
<i>Jeeraka</i>	<i>Cuminum cyminium</i>	Contains phytoestrogens, improves digestion, alleviates <i>Vata</i> indirectly supporting fertility
<i>Bala</i>	<i>Sida cordifolia</i>	Reduce menopausal symptoms, enhances strength
<i>Amalaki</i>	<i>Phyllanthus emblica</i>	Improve the hormonal imbalance, has antioxidants, also supports immune function
<i>Methika</i>	<i>Trigonella foenum</i>	Reduces the severity of Menopausal syndrome, boosts fertility, improves ovulation

<i>Kumari</i>	<i>Aloe barbadensis miller</i>	Improves hormonal imbalance, Reduces the severity of Menopausal syndrome
<i>Yashti Madhu</i>	<i>Glycyrrhiza glabra</i>	Reduces the severity of Menopausal syndrome
<i>Vidari</i>	<i>Pueraria tuberosa</i>	Reduces the severity of Menopausal syndrome
<i>Kumkuma</i>	<i>Crocus sativus</i>	Improve the imbalance
<i>Jayanti</i>	<i>Sesbania sesban</i>	Reduces the severity of menopausal symptoms
<i>Vamsha</i>	<i>Bambusa arudinacea</i>	Mimics the body hormones
<i>Dashamulam</i>		Contains Phytoestrogens
<i>Triphala</i>	<i>Amla- Emblica officinalis</i> <i>Haritaki- Terminalia chebula</i> <i>Vibhithaki- Terminalia bellirica</i>	Contains phytoestrogens
<i>Shata Pushpa</i>	<i>Anethum graveolens</i>	Contains phytoestrogens
<i>Lodhra</i>	<i>Symplocos racemosa</i>	Supports female reproductive health, regulates menses and enhances sexual well being
<i>Gokshura</i>	<i>Tribulus terrestris</i>	Improve libido and female sexual function, help manage PCOS, regulates mensural cycle, supports vaginal health and pH balance
<i>Shilajit</i>	<i>Asphaltum punjabianum</i>	Balances female hormones, regulates mental cycle alleviates PMS syndrome, enhances fertility, supports healthy pregnancy

<i>Brahmi</i>	<i>Bacopa monnieri</i>	Reduces stress and anxiety normalizes hormones, supports cognitive function and mental wellbeing, manage menopausal symptoms like mood swings and memory issues
<i>Putranjivaka</i>	<i>Putranjiva roxburghii</i>	Effective in female infertility and promotes conception
<i>Shivalingi</i>	<i>Bryonia laciniosa</i>	Works well in female reproductive health
<i>Chandraprabha Vati</i>		Effective in <i>Artava Dosa Mootraghata, Yonivyapad</i>
<i>Loha Bhasma</i>		Effective in amenorrhea, leucorrhea, irregular menstrual cycle
<i>Ashoka Arishtam</i>		Possess oestrogenic activity
<i>Choraka</i>	<i>Achyanthes aspera</i>	Has oestrogenic activity
<i>Punarnava</i>	<i>Boerhavia diffusa</i>	Support hormonal imbalance, relieves PMS symptoms, boost fertility & energy levels
<i>Nagakeshara</i>	<i>Meda ferrea</i>	Supports hormonal imbalance, addresses menstrual irregularities, boost fertility
<i>Twak</i>	<i>Cinnamomum verum</i>	Regulates menstrual cycle and improve insulin sensitivity
<i>Shweta Shrinkataka</i>	<i>Clerodendrum serratum</i>	
<i>Kusumba</i>	<i>Carthamus tinctorius</i>	Regulates menses, improves blood circulation and has anti-inflammatory properties

Nagavalli	<i>Piper betle</i>	Regulates menstrual cycles, possesses anti-microbial & anti-inflammatory properties
Atasi	<i>Linum usitassimum</i>	Regulates the hormone levels, reduces menopausal symptoms, improves fertility
Atma Gupta	<i>Mucuna pruriens</i>	Help increase libido, regulates hormones and improves fertility
Raktha Chandana	<i>Pterocarpus santalinus</i>	Alleviates irritation and inflammation associated with menstruation due to its cooling properties
Mudga	<i>Vigna radiata</i>	Rich in proteins, essential nutrients, supports reproductive health
Draksha	<i>Virus venefera</i>	Protects the body from oxidative damage

Duration of consuming phytoestrogens^[11]

For postmenopausal women- duration ranging from 8 weeks to 24 months

- 40 mg twice daily for 12 weeks for post-menopausal women
- In terms of bone health, older women who consume the soy milk for over a year had 2.3 percentage increase in Bone density indicating a longer-term consumption may be beneficial.

CONCLUSION

Phytoestrogens have been found to possess a plethora of health benefits for both males and females. These plant-derived compounds exhibit estrogenic activity, which can lead to a range of positive outcomes. For instance, they have been linked to a reduced risk of osteoporosis, cardiovascular disease, breast cancer, and menopausal symptoms. Furthermore, phytoestrogens have been found to improve cognitive function and memory, particularly in older adults. They have also been associated with a reduced risk of certain cancers and may help alleviate symptoms of

depression and anxiety. Phytoestrogens offer a natural and safer alternative to synthetic estrogens because it is more biocompatible than latter. Synthetic estrogens, prepared in laboratory are potentially harmful with increased risks of cardiovascular disease, including heart attacks, strokes, blood clots and adverse allergic reactions. Phytoestrogens are naturally present in a variety of foods, while the exact mechanisms by which phytoestrogens exert their effects are still being studied. It is clear that they play a significant role in maintaining overall health and well-being.

In terms of application, consuming a balanced diet rich in phytoestrogen-containing foods can help support overall health and reduce the risk of chronic diseases.

Overall, the benefits of phytoestrogens are multifaceted and far-reaching. By incorporating these plant-derived compounds into their diet, individuals can support their overall health and well-being, particularly as they age.

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