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Exploring phytoandrogens: A review of their potential in health and medicine

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ABSTRACT

Classical androgen deficiency occurs in about one out of every twenty adult men. In recent decades, the demand for natural compounds as alternatives to allopathic treatments for hormone deficiencies has grown. Many plants are reported to contain steroidal sex hormones. Phytotherapeutics and nutraceutical agents are suggested as novel alternative strategies and show notable promise in conditions of hypogonadism. Similar to phytoestrogens, the concept of phytoandrogens has also been recognized and valued. Phytoandrogens are a class of plant-derived natural products that exert effects similar to testosterone in animals via androgen receptors. Traditional medicines reported for the treatment of syndromes including impotence, infertility, and erectile dysfunction comprise a large class of phytoandrogen candidates with androgenic activities. Thus, the primary purpose of this review is to critically identify and highlight the natural plants that possess androgen-related compounds.

Keywords: Androgen Deficiency, Herbal medicine, Phytoandrogens, Pharmacology.

INTRODUCTION

Androgens play a vital role in male development, influencing sexual differentiation, secondary male characteristics, and sperm production. The two most important androgens are testosterone (TS) and its metabolite, 5α-dihydrotestosterone (DHT), both of which belong to the steroid hormone group. Testosterone, the primary circulating androgen, is synthesized in the Leydig cells of the testes from cholesterol. This process is regulated by luteinizing hormone (LH), which is secreted by the pituitary gland under the control of gonadotropin-releasing hormone (GnRH) from the hypothalamus. Testosterone, in turn, regulates this system through negative feedback. The production of TS involves multiple steps, beginning with cholesterol transport to the inner mitochondrial membrane by steroidogenic acute regulatory protein (Star). The enzyme P450scc then catalyzes the conversion of cholesterol to pregnenolone, which represents the rate-limiting step in TS synthesis. Additional enzymes, including 3β-hydroxysteroid dehydrogenase and 17β-hydroxysteroid dehydrogenase type 3, further convert pregnenolone into testosterone [1-3].

Interestingly, plants also produce testosterone through a process similar to that in animals. In plant cells, TS is synthesized from cholesterol via the cytoplasmic mevalonate pathway, undergoing a series of enzymatic transformations from pregnenolone to androstenedione and finally to testosterone. However, unlike in animals, where TS functions primarily as a sex hormone, in plants, it affects both reproductive traits—such as flower development and sex determination—and vegetative growth [4, 5]. The biological effects of androgens are mediated through the androgen receptor (AR). While both TS and DHT bind to the AR, they do so with different efficiencies [1]. DHT binds more strongly to the receptor and remains attached longer than TS, making it more potent in certain physiological processes. Interestingly, research has also identified functional human nuclear receptors, including the estrogen receptor (ER) and androgen receptor (AR), in plants, suggesting possible cross-kingdom similarities in steroid signaling mechanisms [6].

Androgen Deficiency

Male infertility is a significant health concern, affecting roughly one in twenty men, with hypogonadism being a key contributing factor. In clinical practice, androgen deficiency can present in different ways, including infertility, sexual dysfunction, general health concerns, or self-reported symptoms. Many infertile men experience specific sperm production disorders, such as azoospermia, severe oligozoospermia, or testicular atrophy, though only a small percentage require testosterone therapy for fertility treatment [7].

Testosterone deficiency, can result from either testicular dysfunction, which disrupts hormone production, or pituitary and hypothalamic disorders, which reduce gonadotropin levels. However, men experiencing erectile or ejaculatory dysfunction are not typically testosterone-deficient. Those with symptoms such as fatigue, anemia, mood disturbances, or osteoporosis should undergo a thorough evaluation, as slight declines in testosterone levels may be linked to other medical conditions or decreased sexual activity rather than a true hormonal imbalance. Additionally, testosterone levels naturally decrease with age, which contributes to andropause, a condition associated with hormonal decline in older men [8].

Several conditions can contribute to androgen deficiency. Genetic disorders, such as Klinefelter's syndrome and Kallmann's syndrome, are well-known causes, along with developmental abnormalities, toxic exposures, and medical treatments that impair testicular function. In some cases, testosterone deficiency can be temporary or partial, often triggered by chronic illnesses, severe infections, certain medications, aging, or delayed puberty. While many cases of hypogonadism remain unexplained (idiopathic hypogonadism), a comprehensive evaluation can help identify treatable causes beyond low testosterone and impaired sperm function [7, 9].

Men with classical androgen deficiency also tend to have smaller prostate volumes and lower prostate-specific antigen levels, which can help distinguish them from individuals with other reproductive or hormonal issues [10].

Testosterone products and its precautions

Testosterone therapy is known to provide quick relief from the symptoms of androgen deficiency. However, treatment failure is often linked to insufficient dosage or inconsistent use, rather than an inappropriate treatment plan. Many patients struggle with adherence, primarily due to discomfort with the method of administration. If symptoms persist despite several weeks of standard injectable testosterone therapy, the cause is unlikely to be testosterone deficiency itself. Over the past decade, the use of testosterone therapy has increased worldwide. While it effectively addresses symptoms of primary and secondary hypogonadism, it can also have negative effects on sperm production, contributing to low sperm count (oligozoospermia), reduced motility, and abnormal sperm morphology [11].

Among the various treatment options, injectable testosterone remains the most widely used and cost-effective. Testosterone esters, such as testosterone enanthate, are delivered in an oil-based solution. To maintain stable hormone levels, weekly injections are preferred, though biweekly injections are often used as a compromise. Extending the time between doses may cause fluctuations in testosterone levels, leading to unpleasant symptoms. For those preferring an oral option, testosterone undecanoate is the only available safe oral androgen, as it does not carry the risk of liver toxicity associated with synthetic 17-α alkylated androgens. However, it is expensive, has low and inconsistent absorption rates, and may cause digestive discomfort [12, 72].

Transdermal testosterone patches serve as an alternative to injections, though their effectiveness is somewhat limited by the need for high daily doses. Since these patches contain absorption enhancers, skin irritation is a common side effect. However, some individuals tolerate them well and find them to be a convenient long-term solution. Other transdermal options, such as testosterone gels, creams, and sprays, are often better tolerated and more cosmetically appealing, but they tend to be more expensive [13, 71].

For a longer-lasting approach, testosterone implants can be used. These small pellets, typically inserted under the skin in areas like the abdomen or buttocks, release testosterone steadily over approximately six months. A standard dose consists of four 200 mg pellets (totaling 800 mg). However, implants may not be ideal for older men who might need to stop testosterone therapy quickly. Reimplantation should be considered only after symptoms of deficiency return and low testosterone levels are confirmed through blood tests [14].

Starting Androgen Replacement Therapy

Androgen Replacement Therapy (ART) should only be considered after a confirmed diagnosis of androgen deficiency and a thorough evaluation to rule out contraindications, such as prostate or breast cancer. Once initiated, the primary objective of ART is to restore and sustain optimal androgen levels in body tissues. This is best accomplished through testosterone supplementation in treatment regimens that closely mimic natural eugonadal testosterone levels, while also prioritizing patient adherence by selecting convenient administration methods. Exogenous testosterone therapy remains the standard treatment for male hypogonadism and is widely regarded as the first-line approach for managing the condition [15]. Given the recent population-level bodecline in TS levels among men [16], the need for strategies to naturally increase TS levels is evident, particularly in populations such as athletes and sedentary adults. Several studies have demonstrated that restoring TS levels alleviates andropause symptoms, including loss of skeletal muscle, depressed mood, increased fat mass, sexual dysfunction, and osteopenia [17]. The risk-benefit ratio of TS replacement therapy has come under scrutiny in recent years. Exogenous TS administration has been linked to potential adverse effects, including prostate cancer, benign prostatic hyperplasia, and cardiovascular events. Without major lifestyle modifications, men diagnosed with hypogonadism will likely require lifelong treatment, similar to individuals with type 2 diabetes [18].

Given these limitations, identifying and refining natural substances for reducing andropause symptoms is of utmost importance. Despite notable progress in recent decades, the full potential of plant-derived compounds as sources of therapeutic agents has yet to be fully realized through traditional screening methods. Medicinal plants are increasingly favored as treatment options for various conditions, with herbs, natural products, and plant-derived chemical compounds accounting for approximately 50% of medications in use worldwide [18].

Ayurveda, the traditional Indian medicinal system, is based on ancient texts that emphasize a natural and holistic approach to physical and mental health. It is one of the world's oldest medical systems and incorporates plant-derived formulations as well as products derived from metals and minerals. Traditional Ayurvedic knowledge provides evidence supporting the use of certain herbs for infertility treatment. Historically, numerous natural products have been regarded as aphrodisiacs and have been used to enhance male sexual health [19]. In recent decades, the demand for natural compounds as alternatives to conventional hormonal treatments has increased significantly [20]. Phytotherapeutics and nutraceutical agents, including certain food-derived compounds, have emerged as promising alternative strategies for managing hypogonadism [21].

Phytochemicals

The vast biological diversity of over 250,000 estimated plant species worldwide contributes to an immense chemical diversity, potentially yielding nearly 1,000,000 phytochemicals with promising applications in drug discovery and development. Phytochemicals, including pigments, alkaloids, terpenoids, flavonoids, phenolics, steroids, and essential oils, form a large group of plant-derived compounds known to support various physiological functions, such as appetite stimulation, growth promotion, endocrine modulation, immunostimulation, and stress relief [22].

Numerous plant-derived natural products, along with the plants that synthesize them, exhibit both preventive and curative properties for human diseases [23]. The recognition of these therapeutic potentials has led to the development of many pharmaceutical products originating from plant sources. Plants possess the ability to generate a diverse range of secondary metabolites, many of which have been utilized as effective treatments for various medical conditions. Over the past two decades, approximately one-quarter of all drugs approved by the U.S.

Food and Drug Administration (FDA) have been derived from plants [24].

Mammalian sex hormones in plant tissues

Mammalian sex hormones, including estrogens, androgens, and progesterone, are part of the steroid family, a group of organic compounds distinguished by their sterane carbon skeleton. The variation in steroid structures among living organisms is influenced by the type and placement of functional groups attached to this core. The discovery of estrogens in plants dates back to 1926, when Dohrn first detected these hormones in plant tissues [25]. Later, in 1989, a broader analysis utilizing radioimmunoassay techniques identified mammalian steroids in 128 plant species across more than 50 families [26]. In plants, steroid hormones often act as intermediates in biochemical pathways. For example, in Digitalis species, progesterone plays a key role as a precursor in the synthesis of cardiac glycosides. Additionally, several enzymes involved in processing progesterone and other pregnane derivatives have been identified in these plants. Notably, some of these enzymes—such as steroid 5α-reductase—are also essential in animal steroid biosynthesis, indicating a degree of functional similarity across biological kingdoms [27, 28].

Research on androgen metabolism in plants, particularly in peas and cucumbers, has revealed that when ^{14}C-labeled androstenedione (AED) is introduced into leaf tissues, it undergoes conversion into testosterone [6]. These observations suggest that plants may possess enzymatic pathways similar to those found in animals for the synthesis and metabolism of androgenic substances [28].

Phytoandrogens: Plant-Derived Androgenic Compounds

Nonsteroidal, plant-derived compounds that mimic or disrupt the normal function of estradiol are known as phytoestrogens. Similarly, compounds that mimic or disrupt the action of TS or DHT are referred to as phytoandrogens. These natural compounds, often found in medicinal plants, serve as precursors to male hormones like TS. Among the identified phytoandrogens, androsterone and progesterone occur in more than 80% of studied plant species, while TS and estrogens (estrone and 17β-estradiol) are present in 70% and 50% of species, respectively. Their occurrence varies across different vegetative and reproductive tissues, changes throughout development, and involves biosynthetic enzymes similar to those in animals [29, 30]

Many phytoandrogens interact with AR, acting as agonists, antagonists, or possessing mixed agonist-antagonist effects. These compounds can either activate or suppress AR-mediated signaling, influencing various physiological processes [30]. Decades of research on steroid biosynthesis and metabolism across plant and animal kingdoms suggest that these compounds are naturally present in both domains and share similar metabolic pathways [28].

Šaden-Krehula et al. (1971) were the first to identify testosterone (TS), along with its epimer epiTS (4-androsten-17α-ol-3-one) and androstenedione (4-androsten-3,17-dione), in plant material, specifically from the pollen of *Pinus sylvestris* (Scotch pine) [31]. Later research further confirmed the occurrence of these steroid compounds, including progesterone (PRG), in the pollen of *Pinus nigra* [32].

Several plant species have been identified as AR agonists, including: *Pinus* species, *Tribulus terrestris, Eucommia ulmoides Oliv., Pausinystalia yohimbe, Ptychopetalum olacoides, Eurycoma longifolia, Ginkgo biloba, Lilium davidii* (lily), *Cynomorii herba, Psoraleae fructus, Ginseng radix et rhizome* and *Salviae miltiorrhizae radix et rhizome* [33]. Additionally, Hartmann et al. [34] described the natural occurrence of steroid hormones in common food sources, detecting TS in potatoes, soybeans, haricot beans, wheat (0.02–0.2 $\mu g \cdot kg^{-1}$), maize, barley, and rhubarb [26] (Simons and Grinwich, 1989). TS has also been found in native plant-based oils, including olive oil, corn oil, and safflower (*Carthamus tinctorius*) oil [35].

Effects of Phytoandrogens on Physiological Processes

The physiological impact of phytoandrogens has been extensively studied in both plants and animals. Research has shown that androstenedione (AED), a precursor of testosterone (TS), promotes callus tissue proliferation and enhances germination and growth in immature embryos of *Arabidopsis thaliana* and winter wheat (*Triticum aestivum*) [36]. Additionally, extracts from *Eucommia ulmoides* Oliv. have demonstrated androgenic properties by competing with TS for binding to the ligand-binding domain (LBD) of the androgen receptor (AR) and weakly stimulating AR transcriptional activity in a dose-dependent manner [37]. Furthermore, AED has been found to enhance reproductive development by increasing the proportion of plants that reach the flowering stage in *Arabidopsis* and wheat [38]. These studies indicate that phytoandrogens not only hold therapeutic potential for humans but also play a significant role in plant growth and reproduction.

Simons and Grinwich [26] analyzed plant tissues and revealed a widespread distribution of androstenone, a steroid hormone, across various plant species. In leaf tissue, androstenone was the most commonly detected androgen, with exceptionally high concentrations (>8000 ng/g dry weight) found in *Sambucus racemosus*, *Coleus blumei*, and *Monstera deliciosa*. Among the analyzed species, *Crassula arborescens* had the highest recorded androgen levels in leaves (3200 ng/g dry weight). In stem tissue, androstenone was again the predominant androgen, though present at lower levels compared to leaves. The highest recorded concentration (7800 ng/g dry weight) was found in the stem of *Cornus stolonifera*, with *Persea americana* also exhibiting high androgen levels. Shoots of *Pilea microphylla* contained elevated androstenone concentrations, while *Pinus banksiana* showed high levels of both androstenone and progesterone, suggesting a unique steroid hormone profile. In male cones, particularly high androstenone levels were detected in *Pinus banksiana* and *Picea glauca*, highlighting the potential role of these androgens in reproductive processes within gymnosperms. Similarly, a high androgen concentration was recorded in the inflorescence of *P. × hortorum*, further indicating that certain reproductive structures may accumulate substantial levels of steroid hormones. These findings suggest that phytoandrogens and steroid-like compounds are widely present across various plant taxa, with potential implications for plant physiology, reproductive function, and interactions with herbivores or other consuming organisms (Table 1).

Various plant species have been analyzed for their androgen content, revealing the presence of steroid hormones or hormone-like compounds in different botanical families [39]. Zeitoun and Alsoqeer [40] reported a notably high TS concentration of 244 ng/g dry weight in *Lilium davidii*, suggesting its strong androgenic potential. Janeczko et al. [41] identified 6.25 ng/g dry weight of androst-4-ene-3,17-dione in winter wheat, a precursor to testosterone, indicating the presence of steroid biosynthesis pathways in cereal crops. Hirotani and Furuya (1974) [42] found 2.2 ng/g dry weight of androgenic compounds in *Nicotiana tabacum* (tobacco), while *Inula helenium* contained 3.2 ng/g dry weight of androgens. Additionally, Kenari [43] reported 5.5–11.4 ng/g dry weight of androstenone in *Pastinaca sativa* L. (parsnip root), a compound known for its role in mammalian pheromone signaling. These findings suggest that androgen-like compounds are present in diverse plant species, potentially influencing hormonal balance, reproductive health, and plant growth regulation.

Wasserman *et al.* [44] investigated the presence of plant compounds that bind to steroid hormone antibodies in immunoassays for various plant species collected in Kibale National Park, Uganda. The study assessed different plant parts, including young leaves, mature leaves, bark, and flowers, for their ability to bind to androgen antibodies, indicating the presence of phytoandrogens or other androgen-like compounds (Table 2). *Celtis durandii* exhibited the highest androgenic activity, particularly in young leaves (207.3), followed by mature leaves (145.1). In general, young leaves of several species (e.g., *Celtis africana, Albizia grandibracteata, and Millettia dura*) demonstrated moderate androgenic activity, suggesting that younger plant tissues might have higher concentrations of active compounds.

Table 1: Estimated concentrations of androstenone and androgens in plant organs [26]

S. No.	Species	Organs	Androgen	Androstenenone
1.	*Populus balsamifera*	Shoot tissue	5300	13000
2.	*Cotoneaster integerrimus*	Leaf tissue	3200	1300
		Ripe fruit	50	5000
3.	*Pelargonium xhortorum*	Inflorescence tissue	2600	5100
		Leaf tissue	540	270
4.	*Plecrranthus oerrendahlii Fries*	Shoot tissue	450	9100
5.	*Philodendron domesticum Bunt.*	Shoot tissue	370	3000
		Leaf tissue	40	4000
		Stem tissue	35	140
6.	*Arctium minus*	Leaf tissue	360	530
7.	*Tradescatltia flutninensis Vell.*	Shoot tissue	250	500
8.	*Caragana arbarescens*	Leaf tissue	230	230
9.	*Sambucus pubens Michx.*	Leaf tissue	73	15000
10.	*Sambucus pubens Michx.*	Shoot tissue	98	980
11.	*Coleus xhybridus*	Leaf tissue	120	14000
12.	*Pilea microphylla (L.) Leibm.*	Shoot tissue	140	14000
13.	*Picea glauca (Moench)Voss*	Inflorescence tissue	220	11000
14.	*Monstera delisiosav*	Leaf tissue	140	8400
15.	*Cornus stolonifera Michx.*	Stem tissue	160	7800
16.	*Alisma triviale Pursh*	Leaf tissue	120	4900
17.	*Pilea cadierei Gagnep*	Leaf tissue	110	4300
18.	*Soleirola soleirolii (Req.) Dandy*	Shoot tissue	220	4300

Table 2: Plant compounds that bind to steroid hormone for various plant species

Plant species	Plant part	Androgen
Celtis durandii	Young leaves	207.3
	Mature leaves	145.1
Spathodea campanulata	Mature leaves	193.5
Balanites wilsoniana	Bark	39.5
Celtis Africana	Young leaves	106.6
Newtonia buchananii	Mature leaves	52.5
Albizia grandibracteata	Young leaves	70.6
Millettia dura	Young leaves	68.3
Erythrina abyssinica	Flowers	9.2
Prunus Africana	Mature leaves	22.1
	Young leaves	48.1
Eucalyptus grandis	Bark	14.4
Spathodea campanulata	Bark	15.5

Table 3: Sex steroid hormone in various species of pin pollen

Pinus silvestris [31]	TS	80
	androst-4-ene-3,17-dione	590
	Epitestosterone	110
Pinus sylvestris (Inflorescence tissue) [26]	Androstenenone	9300
Pinus bungeana [26]	TS	11
Pinus banksiana (Shoot tissue) [26]	TS	620
	Androstenenone	12000
Pinus banksiana (Inflorescence tissue) [26]	TS	270
	Androstenenone	13000
Pinus nigra [32]	TS	90
Pinus nigra (poolen) [50]	TS	80-90
Pinus nigra Ar. [50]	dehydroepiandrosterone	150

Table 3: Occurrence of mammalian sex hormones and related mammalian steroids in selected plants [5] (ng. g dry weight^{-1})

Species	Organs	Androgens	Androstenone
Triticum aestivum L.	Leaf tissue		140-220
Hordeum vulgare L.		41	
Monstera deliciosa Liebm.		140	8400
Zea mays L.		170	
Prunus virginiana L.		140	1300
Brassica campestris L.			250
Crassula arborescens		3200	1300
Daucus carota L.	Stem tissue		310
Urtica dioica L.	Shoot tissue	99	
Thlaspi arvense L.		95	190
Acer negundo L.	Female influorescence tissue,	49	0
Syringa vulgaris L.	Influorescence tissue - early bud	44	180
Bromus inermis	Mature seeds	44	
Brassica napus L.		11	

Table 5a: Occurrence of androgens in plants [70]

Species		plant material	DHEA	TS	AD	DHT
C. vulgaris	Green algae	whole cell material	✓	–	–	–
C. reinhardtii			✓	–	–	–
P. patens	Mosses	gametophyte	✓	✓	–	–
L. clavatum	Club mosses	shoot material	✓	✓	–	✓
A. filiculoides	Ferns		✓	–	–	–
E. arvense	Equisetidae		✓	–	–	✓
G. biloba	Gymnosperms	leaf material	✓	–	–	✓
G. gnetum			✓	–	–	✓

Table 5b: Occurrence of androgens in plants in respective of monocots vs dicots [70]

	Species	DHEA	AD	TS	DHT
Monocots	*Hordeum vulgare*	✓	–	–	–
	Allium schoenoprasum	✓	–	✓	–
	Convallaria majalis	✓	✓		–
	Aspidistra elatior	✓	–		–
	Ruscus aculeatus	–	–	✓	–
	Hyacinthus orientalis	✓	–		–
	Tulipa gesneriana	✓	–	–	–
	Freycinetia cumingiana	✓	–	✓	✓
	Dioscorea bulbifera	✓	–	–	–
Dicots	*Plantago lanceolata*	✓	–	–	✓
	Digitalis grandiflora	✓	–	✓	–
	Olea europaea	✓	–	–	✓
	Arabidopsis thaliana	✓	–	✓	✓
	Erysimum crepidifolium	–	–	✓	–
	Melilotus officinalis	✓	–	–	✓
	V. faba	✓	–	–	–
	Galium odoratum	✓	–	–	✓
	Salix alba	✓	–	✓	✓
	Betula pendula	✓	–	–	✓
	Fagopyrum esculentum	✓	–	–	✓
	Eucalyptus globulus	✓	–	–	✓
	Vaccinium myrtillus	✓	–	–	✓
	Althaea officinalis	✓	–	–	✓
	Rubus fruticosus	✓	–	–	✓

Steroids are detectable at amounts between 0.5 and 10 ng ml^{-1}using the developed UHPLC-ESI-MS/MS method. (✓), steroid was detected; (−), indicates that the analyte was not detectable, that is, no or too low signal ($S/N < 3$) or absence of the respective qualifier signal.

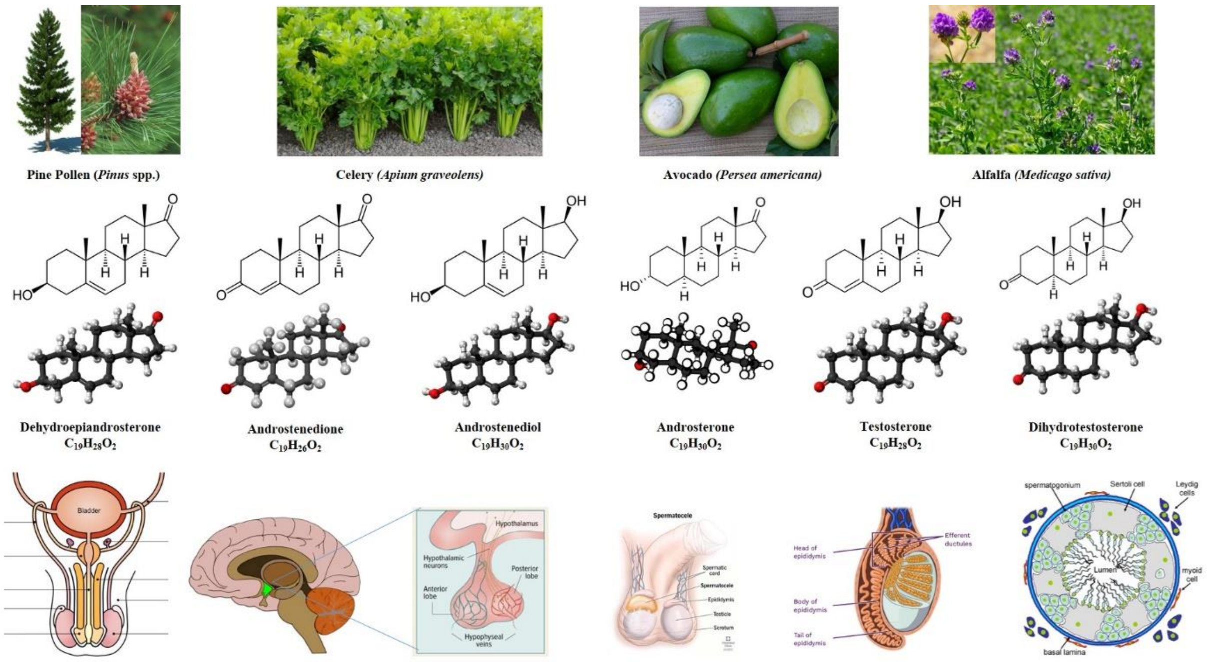

Figure 1: Phytoandrogens on male reproductive health

Pine Pollen: A Natural Source of Phytoandrogens

Pine pollen, a rare natural source of plant-based TS, holds significant potential for the forestry and pharmaceutical industries. It has been consumed for health and well-being in China, South Korea, and Japan for over 3,000 years and remains one of the most underutilized plant-based medicines in modern times. Pine pollen (*Pinus* spp.) is a well-documented Chinese herbal medicine, first recorded in the *Tang Dynasty's Xin Xiu Ben Cao*. Pine pollen is a fine, dry, light-yellow powder released by pine trees every spring as part of their reproductive cycle. It is produced inside catkins (male flowers) of pine species, primarily derived from *Pinus massoniana* Lamb., *Pinus tabuliformis* Carriere, and related species. It is widely regarded as a "natural micronutrient storeroom" due to its rich composition of amino acids, minerals, vitamins, enzymes, and flavonoids [45]. As a dietary supplement, pine pollen has been associated with multiple health benefits, including: Energy enhancement and hormonal balance, Immune system modulation, liver protection, antitumor activity, antioxidant properties, anti-inflammatory effects, anti-aging properties, fatigue reduction and blood lipid and glucose regulation

Pine pollen represents a unique and potent source of phytoandrogens with significant implications for human health, aquaculture, and pharmaceutical applications. Its rich hormonal profile, particularly the presence of testosterone, DHEA, and androstenedione, sets it apart from other plant-based supplements. As research into its androgenic potential continues, pine pollen may emerge as a valuable natural alternative for testosterone supplementation and metabolic enhancement [46]. These naturally occurring androgens are bioavailable, meaning that upon digestion or absorption, pine pollen can rapidly elevate testosterone levels.

Organic dietary hormones found in pine pollen have the potential to enhance profitability in aquaculture by improving growth rates, feed consumption, and food conversion efficiency [47]. *Pinus tabulaeformis* has been effectively used as an alternative to 17α-methyltestosterone in the diet of Nile tilapia larvae, facilitating both sex reversal and growth promotion [48]. Additionally, a phytochemical analysis of *Pinus halepensis* needles identified androstadienedione, a precursor to boldenone, an anabolic steroid [49]. Among plant sources, *Pinus* species are recognized as some of the most potent producers of phytoandrogens.

The androgens present in pine pollen are identical to the hormones naturally produced in the human body. This distinguishes pine pollen as a unique plant-based source of bioavailable testosterone. The average TS level in a healthy adult male is approximately 500 ng per deciliter of blood**.** Given this baseline, the concentration of TS in pine pollen is remarkably high for a food-derived resource.

Pine pollen can be consumed in various forms, but tinctures are considered the most efficient method of administration. Unlike powders, tinctures are directly absorbed into the bloodstream via the oral mucous membranes, bypassing the digestive system for faster bioavailability. Swirling the tincture in the mouth before swallowing enhances its absorption [51, 52]. Both men and women can benefit from consistent or periodic use of pine pollen to support hormone balance and overall well-being.

Beyond providing exogenous testosterone, pine pollen also stimulates endogenous testosterone production by influencing the hypothalamic-pituitary-testicular (HPT) axis**.** It enhances the release of FSH and LH**,** which, in turn, signal the Leydig cells in the testes to synthesize more testosterone. This dual mechanism—direct testosterone supplementation and HPT-axis stimulation**—**positions pine pollen as a powerful natural androgenic and aphrodisiac agent [53].

***Apium graveolens* (Celery)**

Apium graveolens, commonly known as celery, is a marshland plant belonging to the Apiaceae family. It has been cultivated as a vegetable since ancient times and is consumed worldwide in various forms, including its stalks, leaves, and hypocotyl. Celery provides numerous essential nutrients and bioactive compounds that promote overall health, including: detoxificatier**,** minerals (calcium, sodium, copper, magnesium, iron, zinc, and potassium), vitamins (Vitamins A, K, C, D, E, riboflavin, folic acid, B6, B12) and lipid regulators (3-n-butylphthalide). Phthalides help relax artery walls and improve blood flow, reducing hypertension. Its also contains over 25 anti-inflammatory compounds, beneficial for arthritis and osteoporosis. Flavonoids like apigenin and luteolin help treat gastric ulcers and destroy pancreatic cancer cells. Quercetin, a potent flavonoid, reduces swelling and oxidative stress [54].

Celery contains high levels of androstenone and androstenol, male hormones that stimulate sexual arousal in women. When inhaled, these prohormones bind to androgen receptors in the nasal cavity, stimulating the olfactory bulbs and triggering the release of gonadotropin-releasing hormone (GnRH) from the hypothalamus, thereby increasing TS production naturally. Additionally, celery contains androsterone, a steroid hormone that promotes hypothalamic-pituitary activation, further increasing testosterone levels. Celery is also rich in nitrates, which enhance sexual health, making it a potent aphrodisiac food [55, 56].

***Persea americana* (Avocado)**

Persea americana, commonly known as avocado, belongs to the Lauraceae family. Different parts of the fruit have been used for medicinal and therapeutic purposes, though the seed is often discarded despite its rich bioactive potential [57]. Avocado has been widely used in traditional medicine for its various health benefits. Different parts of the avocado tree, including the fruit skin, leaves, and seeds, possess medicinal properties. The fruit skin is traditionally used to treat dysentery due to its antimicrobial and anti-inflammatory effects [58]. The leaf extract has been utilized for managing hypertension, as it contains phenolic compounds that help regulate blood pressure and promote vasodilation [59]. The avocado seed, often discarded, is a powerhouse of bioactive compounds such as phenolic compounds, flavonoids, saponins, tannins, and alkaloids, which exhibit antioxidant, antimicrobial, cardioprotective, and anti-diabetic properties [60]. These bioactive components contribute to the seed's potential role in managing diabetes, cardiovascular diseases, and microbial infections, making avocados a valuable plant in both traditional and modern medicine [61, 62].

Avocado positively impacts male reproductive health due to its rich nutritional profile and bioactive compounds. It contains essential vitamins such as vitamin E, vitamin C, and zinc, which enhance sperm quality by improving motility, count, and morphology while protecting sperm cells from oxidative damage. The healthy monounsaturated fats and vitamin B6 in avocado support testosterone production, aiding in hormone balance and libido [63]. Additionally, its high potassium and folate content promotes healthy blood circulation, which is crucial for erectile function and overall reproductive health. Avocado also contains powerful antioxidants like glutathione and lutein, which reduce oxidative stress and inflammation, protecting the testes and sperm from damage. Additionally, beta-sitosterol found in avocados is known to support prostate health and may contribute to lowering the risk of benign prostatic hyperplasia (BPH), a prevalent condition among aging men [64]. By regulating blood sugar levels through its fiber and healthy fats, avocado also helps prevent metabolic issues that can negatively affect testosterone and fertility. Regular consumption of avocado, combined with a balanced diet and healthy lifestyle, can significantly support male reproductive health, enhance fertility, and reduce the risk of related disorders [65].

Simons and Grinwich [26] investigated the presence of steroid hormone-like compounds in *Persea americana*. They found significant levels in its stem tissue, with values of 830 and 330 (presumably in arbitrary binding units or ng/g dry weight). These findings suggest that avocados contain phytoandrogens or other bioactive compounds capable of interacting with androgen receptors or influencing hormonal activity. The high binding activity observed in avocado stem tissue indicates a potential role in modulating endocrine function, which could impact reproductive health, hormone balance, and metabolic processes in animals or humans consuming avocado-derived products. Compared to other plant species studied for androgenic properties, avocado exhibits relatively high levels of hormone-binding compounds, highlighting its possible influence on testosterone regulation and reproductive physiology [66].

Alfalfa (*Medicago sativa*) and Its Androgenic Properties

Alfalfa is a nutrient-dense legume widely known for its medicinal and nutritional benefits. It contains various bioactive compounds, including phytoestrogens, flavonoids, saponins, and alkaloids, which contribute to its potential androgenic properties. Some studies suggest that alfalfa may influence male reproductive health and hormone regulation by interacting with androgenic pathways. One of the key components of alfalfa is saponins, which have been linked to increased testosterone levels by stimulating LH production. Additionally, alfalfa is rich in zinc, vitamin K, and amino acids, which support testosterone synthesis and overall hormonal balance [67, 68].

Some research suggests that moderate consumption of alfalfa can enhance overall hormonal equilibrium without significantly disrupting androgenic activity. Moreover, its antioxidant properties help combats oxidative stress, which is known to impair testosterone production and sperm quality. Overall, alfalfa may support male reproductive health by promoting hormonal balance, enhancing testosterone production, and reducing oxidative stress [69]. Zeitoun and Alsoqeer [40] investigated the presence of sex steroid hormones in alfalfa (*Medicago sativa*) and native rangeland species in Saudi Arabia, focusing on their effects on camel reproduction. Their study identified significant levels of testosterone in specific forage plants, such as *Cakile arabica* (3.69 ng/g dry weight) and *Cyperus conglomeratus* (2.97 ng/g dry weight). These findings suggest that certain forage plants, including alfalfa, may play a role in modulating reproductive functions through their phytoandrogen content. While alfalfa is widely known for its phytoestrogenic properties, this research highlights its potential androgenic effects, which could impact testosterone levels and reproductive performance in animals

Shiko et al. [70] provided key insights into the presence and role of progestogens, androgens, androstenone, and other androgenic compounds, which may play roles in growth regulation, reproductive processes, and stress responses. One of the major findings was the widespread occurrence of progestogens and androgens in different plant tissues, such as leaves, stems, roots, flowers, and reproductive structures. These compounds were identified in both gymnosperms and angiosperms, suggesting a conserved role in plant metabolism.

LIMITATIONS AND PERSPECTIVES

While phytoandrogens offer a promising natural source of anabolic steroids, it is essential to recognize their limitations. Unlike synthetic injectable steroids, these plant-derived compounds do not provide the same potency or pharmacokinetic profile. Despite some progress in identifying TS and DHT in various plant species, research on their precise distribution remains limited. Scientific studies focusing on the isolation and quantification of these androgens in plants are scarce. The available literature suggests that numerous plant species contain phytoandrogens, with molecular structures closely resembling human androgens. However, functional studies validating their physiological effects are lacking, as indicated by our PUBMED search. Most of the identified phytoandrogen-containing plants have not been extensively studied in biological or clinical settings. Conversely, Indian traditional medicine has a rich history of using herbal therapies for male reproductive health. Several aphrodisiac plants used in Ayurveda have been scientifically studied, showing effectiveness in managing androgen-deficient conditions, including erectile dysfunction, premature ejaculation, menstrual irregularities, kidney yang deficiency, and infertility. For instance, *Withania somnifera* (ashwagandha), *Asparagus racemosus* (shatavari), and *Emblica officinalis* (amla) are widely used for hormone balance and fertility enhancement. However, a significant limitation in the Indian system of natural medicine is that, while many herbs are clinically linked to improved male reproductive health, most studies do not establish the presence of androgenic or phytoandrogenic compounds in these plants.

To bridge this gap, future research should focus on:

- Expanding functional studies on phytoandrogens to confirm their biological effects.
- Isolating and characterizing androgenic compounds in medicinal plants.

- Integrating phytotherapeutic approaches with modern biochemical and clinical evaluations to validate their efficacy in androgen-deficient disorders.

This would enhance our understanding of phytoandrogens and their potential applications in natural medicine.

CONCLUSION

Phytoandrogens hold significant potential in the treatment of androgen deficiency, offering a natural and holistic alternative to conventional therapies. However, their precise mechanisms of action remain largely unexplored, necessitating further research to establish their classification and functional roles. Addressing this knowledge gap is crucial for developing effective treatments for androgen deficiency.

Since different phytoandrogens may target various pathways in prostate and reproductive health, their multi-target and multi-dimensional effects could provide the foundation for more comprehensive treatment strategies in future clinical trials. This review highlights the need for the Indian system of herbal medicine to integrate phytochemical analyses—specifically the quantification of phytoandrogen levels—when investigating male and female reproductive health.

Additionally, the review reveals that numerous plant species contain measurable levels of phytoandrogens. These plants represent a promising avenue for future functional studies aimed at improving sexual and reproductive health. Further research focusing on their bioavailability, efficacy, and clinical applications will be instrumental in advancing the therapeutic use of phytoandrogens in medicine.

Conflict of interest

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