

# From Prostate Health to Hair Loss: A Comprehensive Review of Saw Palmetto's Bioactive Compounds and Clinical Applications

Sravani Thimmannagari\*, Hebbani Nagarajappa Shivaprasad, Gaurav Soni, Madhu Krishnamani

Research and Development Centre, Botanic Healthcare Pvt. Ltd., TSIIIC Industrial Development Area, Nacharam, Uppal, Hyderabad, Telangana, INDIA.

## ABSTRACT

Saw palmetto (*Serenoa repens*) is a palm species with rhizomatous growth, indigenous to the southeastern region of the United States. Traditionally, it has been utilized in herbal medicine for various purposes, with a notable emphasis on supporting men's health. The berries of saw palmetto contain a range of bioactive components, including fatty acids (such as lauric, oleic, myristic, palmitic, and linoleic acids), phytosterols ( $\beta$ -sitosterol, campesterol, and stigmasterol), and flavonoids (rutin, isorhamnetin, quercetin, and astragalin). These constituents play a key role in the plant's diverse biological activities, including its capacity to block 5 $\alpha$ -reductase, the enzyme that facilitates the conversion of testosterone into Dihydrotestosterone (DHT). This inhibition is central to saw palmetto's reported benefits in Benign Prostatic Hyperplasia (BPH) and androgenetic alopecia. Preclinical and clinical studies indicate that saw palmetto extract may help alleviate urinary symptoms related to BPH and support hair health by reducing follicle miniaturization attributed to elevated DHT. Additionally, its anti-androgenic and anti-inflammatory properties appear to add to these therapeutic effects. However, quality control challenges and variable regulatory status exist, given differences in extract standardization and oversight among countries. Overall, available research indicates that standardized extracts of saw palmetto are typically safe and well-tolerated natural option for managing conditions linked to androgen activity, such as BPH and hair loss, though attention to product quality and further research are warranted.

**Keywords:** 5 $\alpha$ -reductase Inhibitor, Alopecia, Benign Prostatic Hyperplasia, Saw Palmetto, Traditional Medicine.

## Corresponding Author

**Mrs. Sravani Thimmannagari**

Manager-Research and Development  
Centre, Botanic Healthcare Pvt. Ltd.,  
TSIIIC Industrial Development Area,  
Plot, 16/1/12 and 13, Nacharam, Uppal,  
Hyderabad-500076, Telangana, INDIA.  
Email: research1@botanichealthcare.com

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## INTRODUCTION

Herbal medicine has long been an integral part of health care across the world, attracting renewed attention in recent years for its therapeutic potential.<sup>[1]</sup> Growing interest in natural remedies has led to a broader movement from synthetic pharmaceuticals toward plant-based treatments—a trend often described as a “Return to Nature.” Medicinal plants are valued for their rich diversity of bioactive compounds, which can play meaningful roles in both preventing and managing disease.<sup>[2]</sup> The significance of herbal medicine is reflected in World Health Organization estimates, which suggest that about 80% of people worldwide depend on traditional plant-based remedies as their main source of health care. This widespread reliance underscores the

continued importance and broad acceptance of herbal medicine in contemporary health practices.<sup>[3]</sup>

The field of phytotherapy has gained significant attention as modern research explores the efficacy, safety, and standardization of herbal medicines. Traditional medicine integrates plant-based therapies with spiritual and physical healing practices, creating a holistic approach to healthcare.<sup>[4]</sup> Herbal medicine or phytomedicine, utilizes plant extracts in various forms such as capsules, pills, powders, liquids, and gels to support health and treat ailments.<sup>[5]</sup> Despite its historical usage, scientific validation remains a key factor in integrating herbal medicines into modern pharmacology. Medicinal plants have contributed to the development of numerous pharmaceutical drugs, with approximately 25% of modern medications originating from botanicals.<sup>[6]</sup>

The use of herbal medicine is increasing not only in developing nations but also in industrialized countries, where a preference for natural and holistic treatments has fueled the growth of the herbal market.<sup>[7]</sup> With the rise in demand for plant-based therapies,



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research efforts have intensified to evaluate the molecular mechanisms and therapeutic efficacy of herbal extracts.<sup>[8]</sup>

Despite its benefits, herbal medicine faces several challenges, including standardization, variability in phytochemical composition, and potential toxicity concerns. The efficacy of herbal remedies is often influenced by factors such as geographical location, cultivation methods, and storage conditions. Moreover, ensuring the authenticity and purity of herbal products remains a significant concern due to the increasing occurrence of adulteration and contamination. Regulatory authorities worldwide are working towards establishing guidelines to address these challenges and enhance consumer safety.<sup>[7,8]</sup>

The integration of herbal medicine with modern healthcare requires a multidisciplinary approach that combines traditional knowledge with scientific advancements. The incorporation of pharmacological, toxicological, and clinical research will help bridge the gap between traditional uses and evidence-based medicine.

Among the many medicinal plants studied for their therapeutic benefits such as *Pygeum africanum*, *Urtica dioica*, *Cucurbita pepo*, and many more, Saw Palmetto (*Serenoa repens*) has gained significant attention for its role in managing Benign Prostatic Hyperplasia (BPH) and other urological conditions.<sup>[9]</sup> Current research has focused on its potential mechanisms of action, clinical efficacy, and safety profile, making it a widely used herbal supplement. This review article provides a comprehensive overview of history, phytochemistry, pharmacology, mechanism of action in prostate and hair health along with safety and toxicity considerations.

## HISTORY

*Sabal serrulata* or *Serenoa repens* has been documented by botanists for only about 200 years. Early accounts by John and William Bartram in the 18<sup>th</sup> century describe palmetto species in Florida, with animals and indigenous peoples relying on their berries for sustenance. A harrowing 1696 shipwreck account by Jonathan Dickinson highlights the berries' role in survival, despite their initially unpleasant taste. Medicinal use of SP was first noted by Dr. J.B. Read of Savannah, in the late 19<sup>th</sup> century, and its therapeutic applications have since expanded. The berries, rich in fats and sugars, were historically gathered in large quantities, with drying techniques influencing their market quality and medicinal properties.<sup>[10]</sup>

## TRADITIONAL USES

Native Americans in the southeastern U.S. used SP as food and medicine, primarily for urinary and reproductive issues like prostate hypertrophy, cystitis, and impotence. The fruit was also believed to boost libido, aid digestion, and act as a nutritive tonic.

Additionally, the plant's leaves, stems, and roots provided fiber and wax. By the early 1900s, SP gained popularity for urinary tract health and reproductive support.<sup>[11,12]</sup>

## SCIENTIFIC CLASSIFICATION

**Table 1: Taxonomical Classification of Saw palmetto.**<sup>[12,13]</sup>

Kingdom	Plantae	Synonyms
Phylum	<i>Streptophyta</i>	<i>Corypha repens</i>
Class	<i>Equisetopsida</i>	<i>Corypha olivacea</i>
Subclass	<i>Magnoliidae</i>	<i>Chamaerops serrulata</i>
Order	<i>Arecales</i>	<i>Sabal serrulata</i>
Family	<i>Arecaceae</i>	<i>Diglossophyllum serrulatum</i>
Genus	<i>Serenoa</i>	<i>Brahea serrulata</i>
Species	<i>S. repens</i>	<i>Serenoa serrulata</i> <i>Serenoa repens</i> f. <i>glauca</i>

## PLANT DESCRIPTION AND HABITAT

It typically grows 3 to 6 feet tall, occasionally reaching up to 15 feet, with prostrate or upright stems extending 10 to 15 feet, and some plants estimated to be 500-700 years old. The palmate leaves, ranging 1.5-3 feet wide, vary in color from green to bluish-green (Figure 1(A)). In spring, it produces insect-pollinated white flowers, followed by bluish-black drupes that ripen from May to October. It thrives in pine flatwoods, scrubby flatwoods, sandy berms, and coastal dunes, growing under shade or full sun. The plant favors sandy, acidic soils like Leon, Myakka, and Immokalee sands, but also occurs on calcareous soils and limestone in southern Florida. It is commonly associated with gall berry, wax myrtle, oaks, wiregrass, and bluestem grasses. SPB are dark drupes that ripen from green to black-purple, with the berries containing a single large seed (Figure 1(B)). The roots typically grow shallow but may extend deep in well-drained soils. Seed germination rates vary, with higher success observed after animal digestion. Rainfall in its habitat ranges from 114 to over 150 cm, with peak precipitation from June to September in the southern part of its range (Figure 1).<sup>[13-15]</sup>

## PHYTOCHEMISTRY

SP contains a complex mixture of phytochemicals that contribute to their therapeutic properties. The phytochemical profile of SP has been extensively studied, revealing several bioactive compounds that may account for its medicinal effects including fatty acids, Phytosterols, flavonoids and polysaccharides.

## Fatty Acids and Phytosterols

The lipophilic extract of SPB contains approximately 70-95% fatty acids.<sup>[16]</sup> The predominant fatty acids include lauric acid, oleic acid, myristic acid, palmitic acid, and linoleic acid.<sup>[17,18]</sup> This specific fatty acid profile distinguishes SP from other medicinal plants and is believed to contribute significantly to its therapeutic effects. The chemical structure of above-mentioned fatty acids is mentioned in the Figure 2.

Phytosterols represent another important class of compounds found in SPB.<sup>[19]</sup> The major phytosterols identified include  $\beta$ -sitosterol, campesterol and stigmasterol (Figure 3).<sup>[20]</sup>

## Flavonoids and Polyphenols

SP contain various flavonoids and polyphenolic compounds that contribute to their antioxidant and anti-inflammatory properties. Rutin, isorhamnetin, quercetin, and Astragalin have been identified in SPE (Figure 4).<sup>[21]</sup>

## PHARMACOLOGICAL BENEFITS

SPE demonstrates multiple pharmacological properties that contribute to its therapeutic potential in various conditions. Its primary mechanisms include inhibition of 5 $\alpha$ -reductase enzyme activity, anti-androgenic effects, anti-inflammatory actions, and anti-proliferative properties.<sup>[22]</sup>

### Benign Prostatic Hyperplasia (BPH)

Benign Prostatic Hyperplasia (BPH) involves a non-cancerous increase in the size of the prostate gland and impacts about half of men by the age of 60, rising to 90% by age 85.<sup>[23]</sup> The condition develops through multifactorial pathogenic processes including aging, hormonal changes, chronic inflammation, and metabolic factors. Central to BPH development is Dihydrotestosterone (DHT), formed when testosterone is converted by the enzyme 5 $\alpha$ -reductase. DHT stimulates stromal and epithelial hyperproliferation, resulting in prostate enlargement.<sup>[24,25]</sup> Saw

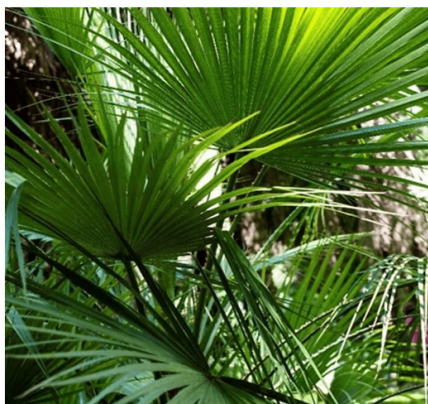
palmetto is particularly relevant in BPH management because it inhibits 5 $\alpha$ -reductase activity, thereby reducing DHT production while demonstrating anti-inflammatory and anti-proliferative properties that directly address key pathophysiological mechanisms of BPH.<sup>[26]</sup>

## SCIENTIFIC EVIDENCE

### *In vitro* studies

Numerous *in vitro* studies have demonstrated SP's effects on prostate cells. Habib *et al.*,<sup>[27]</sup> demonstrated that *Serenoa repens* extract exhibits a distinctive mechanism of action by inhibiting both 5 $\alpha$ -reductase isoenzymes in prostate cells while uniquely preserving PSA secretion. Their research demonstrated that, in contrast to synthetic inhibitors, Saw Palmetto Extract (SPE) suppresses the growth of prostate epithelial cells and triggers apoptosis without disrupting the androgen receptor's interaction with the PSA gene promoter. As a result, PSA remains a reliable biomarker for monitoring prostate cancer, Baron *et al.*,<sup>[28]</sup> reported that SPE selectively triggers programmed cell death in prostate cancer cell lines through mitochondrial pathway activation, demonstrating a unique tissue-specific anticancer mechanism that involves permeability transition pore opening, mitochondrial depolarization, and subsequent cytochrome c release leading to caspase activation. Its potency was comparable to finasteride, achieving 61% enzyme inhibition, indicating strong prostate health-promoting bioactivity.<sup>[29]</sup>

In studies using prostatic cell lines, Saw Palmetto Berry Extract (SPBE) was shown to inhibit cell growth in a dose-dependent manner. The IC<sub>50</sub> values ranged from 20 to 30  $\mu$ L/mL for 267B-1 and BRFF-41T cell lines, while higher concentrations were required to achieve the same effect in LNCaP cells. Additionally, the extract decreased the expression of Cox-2 and Bcl-2, indicating possible anti-inflammatory and pro-apoptotic properties.<sup>[30]</sup> Phytosterol-rich fractions of SPE selectively inhibited prostate stromal cell proliferation by inducing G0/G1 cell cycle arrest and



(A)



(B)

**Figure 1:** Saw Palmetto: (A) Leaves of Saw palmetto (B) Berries of Saw palmetto.



downregulating IGF-1 and EGF expression. In P69 cells, SPE reduced IGF-I-induced Akt phosphorylation and downstream signaling, including cyclin D1 and p70s6k. Additionally, SPE activated proapoptotic JNK, highlighting its potential antiproliferative and proapoptotic role in BPH management.<sup>[31]</sup> SP induced dose-dependent growth arrest and apoptosis in prostate cancer cell lines, with ED<sub>50</sub> values between 2.0-3.3  $\mu$ L/mL. It upregulated p21<sup>waf1</sup> and p53, while downregulating androgen receptor, PSA, and phosphorylated STAT3.<sup>[32]</sup>

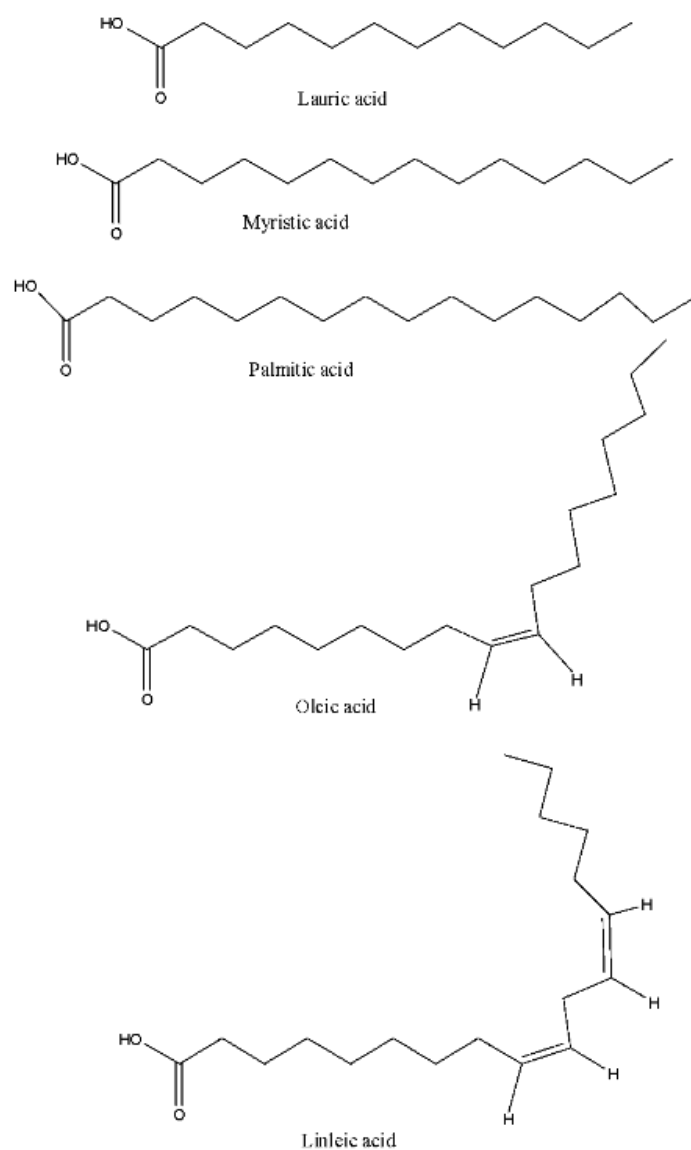
### Animal studies

In a rat model of testosterone-induced BPH,  $\beta$ -sitosterol-enriched Saw Palmetto Oil (VISPO) showed superior efficacy over conventional Saw Palmetto Oil (SPO), significantly reducing prostate weight, serum testosterone, and histological hyperplasia. VISPO also modulated inflammatory and apoptotic protein expression more effectively, suggesting enhanced therapeutic potential for BPH management.<sup>[33]</sup> In a separate study, rats that received oral doses of LSEsr exhibited a marked reduction in prostatic smooth muscle contractions.<sup>[34]</sup> Cao N *et al.*, 2006 explored the effects of SPE on rat prostate contractility and revealed that it induces  $\alpha$ 1-adrenoceptor-mediated contractions via indirect stimulation of noradrenaline release from sympathetic neurons. The contractile effect was attenuated by adrenergic blockers like prazosin and phentolamine, confirming the involvement of the sympathetic pathway.<sup>[35]</sup>

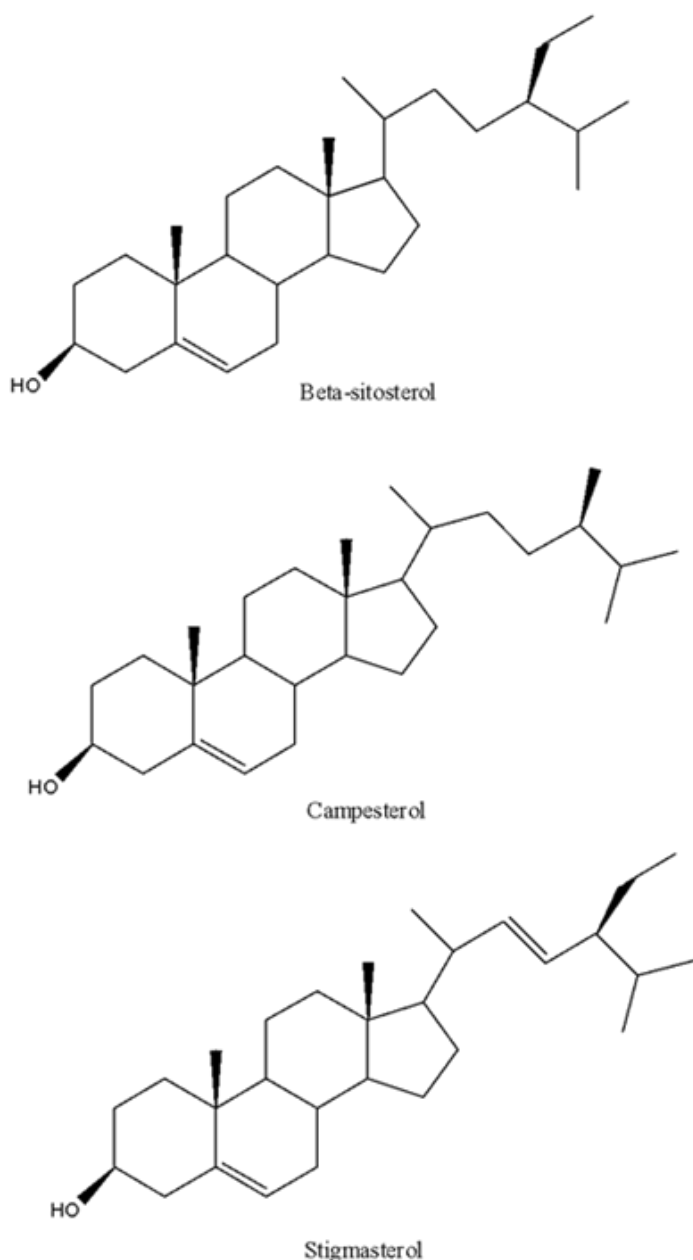
### Clinical data

In a clinical pilot study involving 82 men with mild to moderate BPH showed that daily intake of 320 mg saw palmetto extract for 8 weeks significantly improved urinary symptoms, sexual function, and quality of life. The treatment was well tolerated and positively assessed by both patients and investigators, indicating its dual benefit in managing BPH and associated sexual dysfunction.<sup>[36]</sup> In another 6-month randomized trial involving 1,098 men with moderate BPH, 320 mg of *Serenoa repens* significantly improved symptoms, quality of life, and urinary flow, comparable to finasteride. Additionally, it was also better tolerated, highlighting its potential as an effective alternative for BPH management.<sup>[37]</sup> In an experimental case study involving a 67-year-old male with symptomatic BPH, treatment with standardized SPE at a dosage of 160 mg twice daily led to an improvement in AUASI scores from 20 to 7, along with a decrease in prostate volume from 92 mL to 75 mL. The treatment was well tolerated and effective, while placebo showed less improvement.<sup>[38]</sup> A separate randomized, double-blind, placebo-controlled trial with 144 men diagnosed with BPH demonstrated that a three-month course of natural supplements-including cernitin, saw palmetto,  $\beta$ -sitosterol, and vitamin E-resulted in significant reductions in nocturia, daytime urinary frequency, and overall AUA Symptom Index scores

compared to placebo. The treatment was well tolerated with no significant adverse effects, supporting its potential as a safe and effective option for symptom relief in BPH.<sup>[39]</sup> In a randomized, placebo-controlled trial involving 44 men with symptomatic BPH, a SP herbal blend was found to be safe and well tolerated. Although clinical improvements were not significantly different from placebo, the treatment led to significant epithelial contraction in the prostate transition zone and an increase in atrophic glands, suggesting potential histological benefits that may underlie its clinical effects observed in other studies.<sup>[40]</sup> In a 12-week randomized trial involving 99 men with BPH (33 per group), daily intake of 500 mg  $\beta$ -sitosterol-enriched SP oil significantly improved IPSS, urinary flow rates, and serum free testosterone levels compared to conventional oil and placebo. It also reduced PSA, postvoid residual volume, and 5 $\alpha$ -reductase levels, showing good tolerability and symptom relief.<sup>[41]</sup>



**Figure 2:** Chemical Structures of fatty acid present in SPE.



**Figure 3:** Phytosterols present in Saw palmetto.

### Meta analysis and systemic reviews

This meta-analysis of 27 studies ( $n=5,800$ ) showed that the hexanic extract of *Serenoa repens* (HESr) significantly reduced nocturia, improved urinary flow ( $Q_{max}$ ), and lowered IPSS scores. Its efficacy was comparable to tamsulosin and short-term 5-ARIs, without negatively affecting sexual function. HESr demonstrated good long-term tolerability and a favorable safety profile, supporting its use as an effective treatment for LUTS/BPH.<sup>[26]</sup> A systematic review of 218 papers, including meta-analyses and RCTs, examined the efficacy and safety of SP in treating BPH. The analysis involved 10,601 patients and found that SP was as effective as tamsulosin and finasteride in improving urinary symptoms, flow measurements, and the International Prostate Symptom Score. It also reduced nocturia and increased

peak urinary flow rate, with minimal side effects.<sup>[42]</sup> A systematic review and meta-analysis of 18 randomized controlled trials, encompassing 2,939 men with symptomatic BPH, revealed that SP led to significant improvements in urinary symptoms, decreased nocturia, and enhanced peak urinary flow relative to placebo. It provided similar improvements in urinary tract symptoms and flow rate when compared to finasteride. These findings support *S. repens* as a well-tolerated and effective short-term therapeutic option for BPH.<sup>[43]</sup> The systematic review analyzed 21 studies involving 1,666 patients and found that SP provides symptom relief in chronic prostatitis/chronic pelvic pain syndrome. While monotherapy showed benefits over placebo, the extract was most effective when used in combination.<sup>[44]</sup>

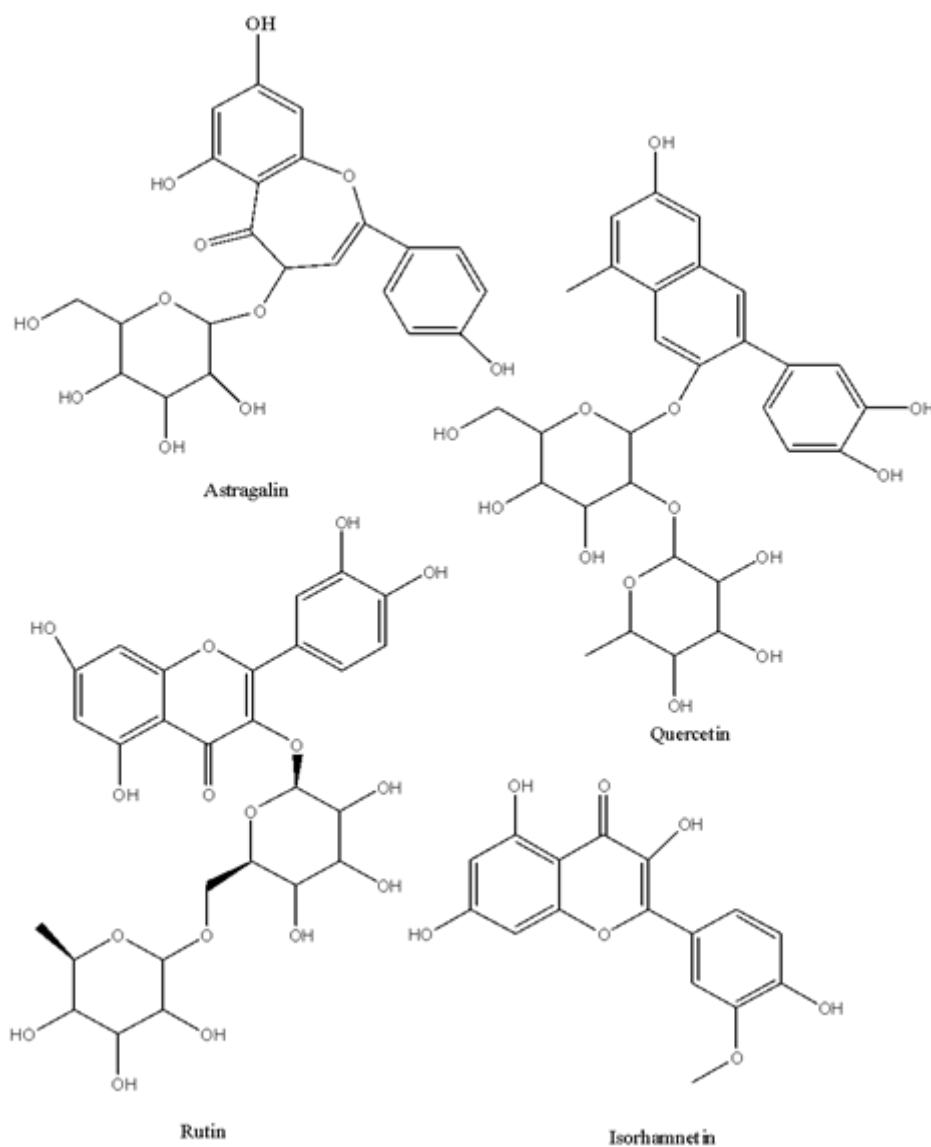
### Hair Health and Androgenetic Alopecia (AGA)

Androgenetic Alopecia (AGA), commonly referred to as male pattern baldness, is a hereditary disorder marked by the gradual shrinking of androgen-responsive hair follicles in specific areas of the scalp. A key biochemical contributor to AGA is the enzymatic conversion of testosterone to DHT by 5 $\alpha$ -reductase. DHT, a more potent androgen, binds to receptors in susceptible hair follicles, triggering a cascade that shortens the anagen (growth) phase, leading to progressively finer and shorter hairs until follicular activity ceases. This same DHT-mediated mechanism is also implicated in the development and progression of BPH.<sup>[45-47]</sup>

*In vitro* experiments using human keratinocyte cells stimulated with lipopolysaccharide showed that the composition significantly suppressed inflammatory gene expression, including chemokines like CCL17, CXCL6, and LTB4. These results support the compound's anti-inflammatory action and suggest that combining 5- $\alpha$  reductase inhibition with inflammation blockade could offer a more effective strategy for treating AGA.<sup>[48]</sup>

In a 16-week double-blind study involving 80 adults with mild-to-moderate androgenetic alopecia, daily intake of 400 mg or topical application of 20% saw palmetto oil (2-3%  $\beta$ -sitosterol) significantly reduced hair fall (up to 29%), improved hair density (up to 7.61%), and lowered serum DHT levels without serious side effects, supporting its safety and efficacy in hair loss management.<sup>[49]</sup> An open-label study evaluated a lotion containing pure Saw Palmetto extract for treating Androgenetic Alopecia (AGA) in 20 men over 12 weeks. Participants applied the lotion twice daily, resulting in a significant increase in mean hair count from 49.8 to 55.9. By week 12, 83% reported high satisfaction, and no adverse effects were noted. The findings suggest the lotion is effective and well-tolerated, though larger, longer-term studies are needed.<sup>[50]</sup>

A placebo-controlled, double-blind pilot study evaluated the effectiveness of plant-based 5 $\alpha$ -reductase inhibitors—specifically LSESr and  $\beta$ -sitosterol—in the treatment of AGA among healthy men aged 23 to 64 experiencing mild to moderate hair loss. Given the shared role of DHT in both AGA and BPH, and



**Figure 4:** Chemical structures of flavonoids and Polyphenols present in Saw palmetto.

previous evidence of these botanicals' effectiveness in BPH, their use in AGA was explored. Results showed that 60% of participants receiving the active formulation demonstrated clinical improvement. This study provides preliminary evidence supporting the therapeutic potential of natural 5AR inhibitors in AGA and warrants larger-scale trials.<sup>[47]</sup>

In a 24-month open-label study on 100 men with mild to moderate AGA, 38% of those treated with SP (320 mg/day) showed increased hair growth, compared to 68% in the finasteride group (1 mg/day). SP showed modest improvement, mainly in the vertex region. Both treatments were well tolerated.<sup>[51]</sup> A review of five randomized controlled trials and two cohort studies demonstrated that oral and topical SP supplements (100-320 mg daily) effectively improved hair growth outcomes in individuals with AGA and telogen effluvium. The findings revealed a 60% enhancement in overall hair quality, a 27% rise in total hair count,

and increased hair density in 83.3% of participants. Furthermore, 52% of individuals saw a halt in the progression of hair loss. Saw palmetto was well tolerated, with no serious adverse events reported, supporting its potential as a promising natural approach for managing hair loss.<sup>[52]</sup>

### Pharmacological benefits beyond prostate and hair health

Date Palm Seed (DPS) and Saw Palmetto (SP) seed extracts exhibited significant antioxidant effects in both DPPH and ABTS assays. These extracts also demonstrated strong antibacterial and antifungal activity against drug-resistant microbes.<sup>[53]</sup> The study investigated the effects of SPE on erectile function in rats and rabbits. SPE was administered at varying doses for 7 days, and results showed a dose-dependent enhancement in corpus cavernosum relaxation during nerve stimulation, similar to sildenafil. SPE significantly inhibited Phosphodiesterase 5

(PDE5) activity and increased iNOS mRNA expression. These findings suggest that SPE may improve erectile function by enhancing nitric oxide signaling and inhibiting PDE5, indicating its potential for treating erectile dysfunction.<sup>[54]</sup> The study evaluated the efficacy and safety of SPBE in treating Lower Urinary Tract Symptoms (LUTS) in women over 12 weeks. SPE significantly reduced daytime urinary frequency and nocturia, particularly in women with more severe baseline symptoms. Improvements were noted in both CLSS and OABSS scores.<sup>[55]</sup> A 28-day study in healthy men (30-59 years) evaluated a supplement containing androstenedione, DHEA, SP, and other herbs. While the supplement significantly increased serum free testosterone, androstenedione, dihydrotestosterone, and estradiol. Total testosterone and PSA remained unchanged, and HDL-C levels decreased.<sup>[56]</sup>

## MECHANISM OF ACTION

SP primarily works through inhibition of 5 $\alpha$ -reductase enzymes, which convert testosterone to the more potent Dihydrotestosterone (DHT).<sup>[29]</sup> In BPH, this inhibition reduces DHT levels in prostate tissue, decreasing prostate cell proliferation and volume.<sup>[57]</sup> Studies have demonstrated that SPE competitively binds to 5 $\alpha$ -reductase types I and II.<sup>[58,59]</sup> These combined actions help alleviate urinary symptoms associated with BPH by reducing prostate enlargement and associated inflammation.<sup>[60]</sup>

For hair health, SP's 5 $\alpha$ -reductase inhibitory activity plays a central role in preventing AGA.<sup>[51]</sup> By blocking DHT formation in hair follicles, it helps prevent miniaturization of follicles and prolongs the anagen (growth) phase of the hair cycle.<sup>[47-61]</sup> SP also contains phytosterols and fatty acids that may improve scalp circulation and provide anti-inflammatory benefits to the hair follicle microenvironment.<sup>[62]</sup> Its anti-inflammatory properties extend beyond the scalp and prostate, with research suggesting systemic effects through modulation of Nuclear Factor- $\kappa$ B (NF- $\kappa$ B) pathways and reduction of pro-inflammatory eicosanoids such as prostaglandins and leukotrienes.<sup>[63,64]</sup> These mechanisms collectively contribute to SP's therapeutic potential in conditions characterized by inflammation and androgen sensitivity.

## SAFETY, TOXICITY, AND REGULATORY STATUS

*In vitro* genotoxicity and cytotoxicity studies of SPE have not revealed any mutagenic or overt toxic effects. For example, *in vivo* assays in mice showed no increase in DNA damage or micronuclei after feeding saw palmetto, apart from minor dose-dependent changes in nuclear chromatin configuration.<sup>[65]</sup> Similarly, standard bacterial mutagenicity (Ames) tests on representative LSESr have been reported as negative (no evidence of mutagenic potential) by regulatory sources, and cell culture assays confirm that SPE does not significantly reduce viability of normal prostatic cells

at pharmacologically relevant concentrations. In a comparative prostate cell study, treatment with *S. repens* (alone or combined with *Urtica dioica*) at 1-20  $\mu$ g/mL for up to 72 hr produced no cytotoxicity in Benign Prostatic Epithelial (BPH-1) or Prostate Cancer (PC3) cells. Thus, current *in vitro* evidence suggests that SP does not exert direct cytotoxic or DNA-damaging effects.<sup>[66]</sup> Extensive animal toxicity tests likewise demonstrate a wide margin of safety. In rodents, no adverse systemic effects were observed even at multi-fold human doses: for instance, rats given 2 $\times$  or 5 $\times$  the maximum recommended human dose of SPE (9.14 or 22.86 mg/kg/day) for 2-4 weeks showed no significant changes in body weight, liver enzyme activities, or lipid peroxidation markers.<sup>[67]</sup> A 3-month oral study in dogs with BPH, using doses up to 1,500 mg/day, showed no adverse effects.<sup>[68]</sup>

Human clinical trial data and post-marketing surveillance corroborate this benign safety profile. Randomized controlled trials in men with BPH have consistently found that SPE is as well tolerated as placebo. For example, the STEP trial (320 mg/day for 6 months) and the CAMUS trial (escalating 320 $\rightarrow$ 960 mg/day for 18 months) reported no significant differences between SP and placebo in overall adverse event rates, serious adverse events, vital signs, laboratory tests or withdrawal rates.<sup>[69,70]</sup> A large multicenter trial in Chinese men (320 mg/day for 24 weeks) similarly found that only about 1-2% of subjects in each group experienced any adverse event, with no significant treatment-related issues.<sup>[71]</sup> Recent meta-analyses (Cochrane 2023) confirm that pooled adverse-event rates do not differ between saw palmetto and placebo (RR $\approx$ 1.01, 95% CI 0.77-1.31).<sup>[72]</sup> In summary, *Serenoa repens* is generally well tolerated, with a toxicology profile that supports its long-term use in men for BPH-related symptoms.

In the United States, SP is regulated as a dietary supplement rather than a drug; manufacturers may make general "structure/function" claims (e.g. "supports prostate health"), but no FDA-approved health claims for BPH exist.<sup>[73]</sup> In contrast, in Europe SP is treated as an herbal medicinal product. The EMA's Committee on Herbal Medicinal Products (HMPC) issued a monograph (2013) recognizing SPE for the symptomatic treatment of BPH. This EU monograph recommends a daily dose of about 320 mg of a lipophilic extract (e.g. 160 mg twice daily).<sup>[74,75]</sup> In Canada, saw palmetto is authorized as a Natural Health Product indicated to relieve LUTS. Health Canada's monograph specifies either 1-4 g/day of dried fruit or 100-400 mg/day of a standardized liposterolic extract.<sup>[76]</sup> In ARTG regulates SP as a listed complementary medicine; labels may only claim traditional uses (e.g. "maintains/supports prostate health"). ARTG-listed products typically deliver on the order of 3-4 g dried fruit equivalent per day.<sup>[77]</sup> Under the FSSAI, SP is listed among botanical ingredients permitted in health supplements.<sup>[78]</sup> No country defines an official "recommended dietary allowance" for SP. however, all monographs agree on a typical therapeutic dose  $\approx$ 320 mg/day of extract for BPH.



## ADULTERATION ISSUES AND QUALITY CONTROL

Recent research indicates that Saw Palmetto (SP) supplements are often at risk of economically motivated adulteration. Common fraudulent tactics include replacing genuine saw palmetto berries with those from related palm species, or diluting authentic lipidosterolic extracts with cheaper vegetable oils or specially formulated “designer” fat blends, some of which may contain animal-derived fatty acids designed to resemble SP’s fatty acid profile. While these adulterants are generally not toxic, they significantly reduce the concentration of active components, such as fatty acids and phytosterols, thereby diminishing the product’s effectiveness.

To prevent such adulteration, a range of complementary quality control methods are employed. Official pharmacopeial monographs set out essential identity tests and compositional standards for SP raw materials and extracts. Sophisticated analytical techniques-including GC-FID/MS for profiling fatty acids and sterols, HPLC fingerprinting, and TLC-are used to accurately measure these key markers. Additionally, untargeted metabolomic methods, such as NMR-based metabolite profiling, have proven useful. For example, NMR can differentiate SP extracts based on solvent type and readily identify abnormal or adulterated samples.<sup>[16-79-83]</sup> At the genetic level, DNA barcoding of plant material provides definitive species authentication Little and Jeanson found that ~85% of tested products contained true *S. repens*, ~6% contained closely related palms, and ~9% were inconclusive.<sup>[79-81]</sup> In a sophisticated, Perini *et al.*, combined fatty-acid profiling with stable-isotope analysis to reveal that many commercial SP oils actually contained significant animal-derived fats.<sup>[82]</sup> Beyond analytical chemistry, regulatory and supply-chain measures enhance authenticity: industry adherence to GMP, chain-of-custody documentation, and certifications helps ensure traceability. Indeed, products made under strict herbal-medicine regulations have been shown to be consistently authentic.<sup>[83]</sup> In conclusion, ensuring product integrity and effectiveness against saw palmetto adulteration relies on strict adherence to pharmacopeial standards and the integration of DNA analysis, chromatographic, and spectroscopic techniques, all within a comprehensive regulatory and traceability framework.

## CONCLUSION

SP is a scientifically supported herbal treatment, with its primary benefit stemming from the inhibition of 5 $\alpha$ -reductase-an enzyme central to the development of both BPH and AGA. The therapy’s effectiveness can be largely attributed to its unique composition of fatty acids and phytosterols. Clinical studies show that standardized SPE effectively relieve BPH symptoms, with results comparable to those of conventional medications but with a better safety profile, especially concerning sexual side effects. Additionally, research suggests that saw palmetto may support

hair health, offering benefits through both oral and topical applications.

Saw palmetto’s action isn’t limited to blocking 5 $\alpha$ -reductase; it also possesses anti-inflammatory, antioxidant, and anti-proliferative properties, making it a multi-targeted approach for androgen-mediated conditions. However, ensuring consistent product quality remains a challenge, highlighting the need for strict quality control standards. Moving forward, future research should prioritize refining extraction processes and expanding clinical trials to further clarify its benefits. Overall, standardized saw palmetto extract stands out as a well-established, evidence-based, and safe alternative for managing conditions driven by androgen activity.

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## ABBREVIATIONS

**SP:** Saw Palmetto; **SPE:** Saw Palmetto Extract; **BPH:** Benign Prostatic Hyperplasia; **AGA:** Androgenetic Alopecia; **DHT:** Dihydrotestosterone; **LUTS:** Lower Urinary Tract Symptoms; **SPO:** Saw Palmetto Oil.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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