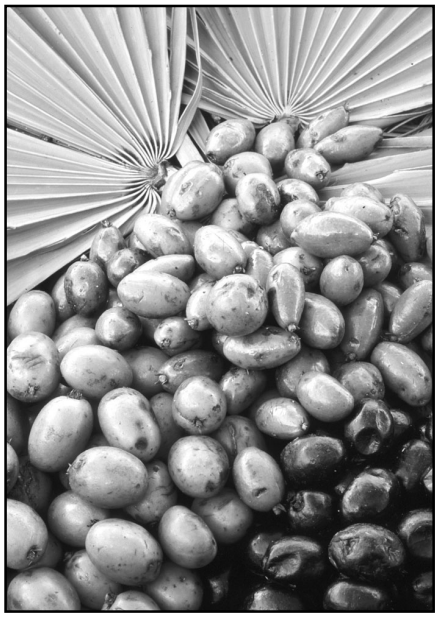
Saw Palmetto

Serenoa repens **(W. Bartram) Small (syn.** ***Sabal serrulata*** **[Michx.] Nutt. ex Schult. & Schult. f.;** ***Serenoa serrulata*** **(Michx.) G. Nichols.)**

[Fam. *Arecaceae*]

Overview

Since the mid-1990s, saw palmetto has been one of the 10 top-selling herbs in the U.S. Total sales in mainstream retail stores in 2000 in the U.S. were over $43 million, ranking saw palmetto sixth in total herb sales. In Europe, saw palmetto extract is the most commonly used phytotherapeutic agent for benign prostatic hyperplasia (BPH) and it is one of the most frequently prescribed botanical preparations in Germany. Saw palmetto berry was commonly recommended for various prostatic conditions by healthcare professionals in the early part of the 20th century. It was an official drug, listed in the *United States Pharmacopeia* from 1906 to 1916 and in the *National Formulary* from 1926 to 1950. In the 20th century, the *United States Dispensatory*, 23rd edition, included saw palmetto as a treatment for enlargement of the prostate gland.



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Primary Uses

- Benign prostatic hyperplasia (BPH), Stages I and II

Pharmacological Actions

Anti-estrogenic activity; increases urinary flow rate; decreases residual urine; decreases painful urination; decreases nocturia.

Dosage and Administration

Research suggests that 4–6 weeks are needed for therapeutic effect to manifest.

Cut fruit and other equivalent galenical preparations: 1–2 g.

Crude berries: 10 g, twice daily.

Fluid extract: 1–2 ml twice daily [1:1 (*g/ml*)]; 2–4 ml twice daily [1:2 (*g/ml*)].

Soft native extract: 160 mg twice daily or 320 mg once daily [10:1–14:1 *(w/w)*, containing approximately 85–95% fatty acids].

Dry normalized extract: 400 mg twice daily [4:1 (*w/w)* contains ca. 25% fatty acids].

Tea: Not effective because the lipophilic active constituents are insoluble in water.

Note: Most clinical studies have been conducted with native extract.

Contraindications

Saw palmetto is contraindicated in advanced BPH with severe urinary retention. It should not be used without first ruling out prostate cancer.

Pregnancy and Lactation: Due to potential hormonal activity, saw palmetto is not recommended for pregnant or lactating women, although the herb is seldom used by women.

Adverse Effects

Gastrointestinal disturbance occurs rarely. Ingestion of large amounts of saw palmetto berries may cause diarrhea, while ingestion of saw palmetto on an empty stomach may cause nausea. Hypertension was reported in 3.1% of patients taking the saw palmetto extract Permixon® (a proprietary saw palmetto extract from France) although this effect is not usually observed in other trials or case studies on saw palmetto. The general safety profile of saw palmetto is superior to that of finasteride. Sexual dysfunction was less common with saw palmetto and the herb has not been associated with erectile dysfunction, ejaculatory disturbance, or altered libido. Gastrointestinal disturbances, urinary tract infections, ejaculation problems, and impotence were reported in 2% of patients taking saw palmetto in a three-year trial.

Drug Interactions

There are no confirmed interactions with saw palmetto. Most clinical trials excluded men taking diuretics, alpha blockers, and anticoagulants; thus, the potential for drug-herb interaction cannot be dismissed. A review of the literature does not reveal evidence of adverse drug interactions between saw palmetto and conventional drugs.

Clinical Review

In nineteen studies that included 7,210 participants, all but two demonstrated positive effects for benign prostatic hyperplasia (BPH). Numerous studies revealed that saw palmetto improved symptoms of BPH including one randomized, single-blind, placebo-controlled, parallel group multicenter study (R, SB, PC, PG, MC), two open-label (OL), MC studies, a R,

double-blind (DB), controlled study, a R, comparative study, a prospective MC study, and a R, PC study. Two OL studies found positive results, but another OL study failed to find significant improvement in objective measures of bladder outlet obstruction. Similarly, one DB, C study found no difference between saw palmetto and placebo. Several clinical trials have shown that serum levels of testosterone, dihydrotestosterone (DHT), and PSA are not changed significantly. One PC study looked at hormone levels, found no changes in testosterone, luteinizing hormone (LH), or follicle stimulating hormone (FSH) levels.

It is well accepted that at least 30–50% of BPH patients report an improvement of their symptoms after treatment with placebo. This percentage is about the same after simple monitoring. Two meta-analyses of 18 R, PC studies concluded that saw palmetto treatment for at least 30 days improved urologic symptoms and flow measures. Adverse effects were mild and infrequent. The authors concluded that further research is needed using standardized preparations to determine saw palmetto's long-term effectiveness and ability to prevent BPH complications. Another meta-analysis focused on 11 R clinical trials and 2 OL trials using saw palmetto extract on men with BPH. The analysis concluded that saw palmetto, compared to placebo, provided a significant improvement in peak urinary flow rate and reduction in nocturia.

Some anecdotal reports have stated that saw palmetto can mask prostate cancer by lowering PSA levels. However, several large studies totaling 1,256 patients did not show this effect.

A meta-analysis of recent PC trials included 7 clinical studies. All trials lasted 3 months and indicated a decrease in nocturia frequency (0.5 times per night) and an increase in peak urinary flow rate by 1.5 ml/sec over placebo. A 6-month, DB, PC, R study comparing Permixon® and finasteride (Proscar®) included 1,809 patients with BPH, and showed equally improved symptom score in both groups (37% with Permixon® vs. 39% with finasteride), and equally improved peak urinary flow rate. One of the first trials conducted in the U.S. reported symptomatic, but not urodynamic, improvement in 46 men treated for 6 months with a saw palmetto berry extract.

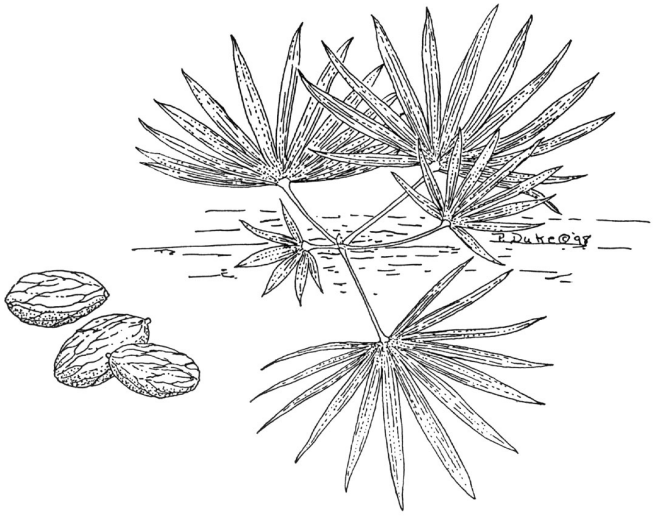
Five studies focused on the use of the combination of saw palmetto and nettles to treat the symptoms of BPH. Originally, it was thought that saw palmetto relieved the symptoms associated with an enlarged prostate without reducing the enlargement. However, one R, DB, PC study on the Nutralite® product examined the use of a saw palmetto, nettles, lemon bioflavonoid extract, and vitamin A combination and found significant improvement in prostate epithelial contraction without adverse effects. Further studies are needed to confirm the finding. Another trial on the same saw palmetto combination product suggested a significant reduction in prostate tissue DHT levels, as determined by needle biopsy. Four well-designed studies on the fixed combination, PRO 160/120®, ranged from 12 weeks to one year, and found good efficacy and tolerance.

Saw Palmetto

Serenoa repens (W. Bartram) Small
[Fam. *Arecaceae*]

Overview

Saw palmetto berries were first used by Native Americans as a diuretic and sexual tonic, as well as for stomachache and dysentery. Since the mid-1990s, saw palmetto has been one of the 10 top-selling herbs in the U.S. Total sales in mainstream retail stores in 2000 were over $43 million, ranking saw palmetto sixth in herb sales.



Uses

Mild to moderate benign prostatic hyperplasia (BPH); enlarged prostate, Stages I and II.

Dosage

4–6 weeks are needed for effectiveness.

CRUDE BERRIES: 10 g, twice daily.

FLUID EXTRACT: 1–2 ml, twice daily [1:1 (*g/ml*)]; 2–4 ml, twice daily [1:2 (*g/ml*)].

SOFT NATIVE EXTRACT: 160 mg, twice daily or 320 mg once daily [10:1–14:1 *(w/w)*, contains approximately 85–95% fatty acids].

DRY NORMALIZED EXTRACT: 400 mg, twice daily [4:1 (*w/w)* contains ca. 25% fatty acids].

NOTE: Most clinical studies have been conducted with the native extract standardized to approx. 85–95% fatty acids.

Contraindications

Saw palmetto should not be used by individuals with advanced BPH and severe urinary retention without first consulting with a healthcare provider to rule out prostate cancer.

PREGNANCY AND LACTATION: Due to potential hormonal activity, saw palmetto is not recommended for pregnant or breast-feeding women, although the herb is seldom used by women.

Adverse Effects

Gastrointestinal disturbance occurs rarely. Ingesting large amounts of saw palmetto berries may cause diarrhea while ingesting saw palmetto on an empty stomach may cause nausea. High blood pressure occurred in only 3% of patients who took saw palmetto extract in a large clinical trial of 951 men although this effect is not normally associated with the use of saw palmetto. Compared to finasteride, the leading prescription drug for BPH, saw palmetto extracts have a better general safety profile and produce less frequent sexual complaints. Saw palmetto has not been associated with erectile dysfunction, ejaculatory disturbance, or altered libido, as can occur with some men using prescription medications for BPH.

Drug Interactions

There are no known interactions between saw palmetto and conventional drugs.

Comments

When using a dietary supplement, purchase it from a reliable source. For best results, use the same brand of product throughout the period of use. As with all medications and dietary supplements, please inform your healthcare provider of all herbs and medications you are taking. Interactions may occur between medications and herbs or even among different herbs when taken at the same time. Treat your herbal supplement with care by taking it as directed, storing it as advised on the label, and keeping it out of the reach of children and pets. Consult your healthcare provider with any questions.

Saw Palmetto

Serenoa repens (W. Bartram) Small (syn. *Sabal serrulata* [Michx.] Nutt. ex Schult. & Schult. f.; *Serenoa serrulata* (Michx.) G. Nichols.

[Fam. *Arecaceae*]

Overview

Saw palmetto is a small, low-growing, dwarf-palm tree, native to southeastern North America, particularly Florida. The berries were a staple food and medicine of the indigenous Floridians before the Europeans' arrival (Duke, 1985; Vogel, 1970). Indigenous Americans prepared an aqueous infusion of the berries to treat stomachache and dysentery (Duke, 1985). They also used the fruit as a diuretic and sexual tonic (Duke, 1985). Since the mid-1990s, saw palmetto has been one of the ten top-selling herbs in the U.S. (Blumenthal *et al.*, 1998; Blumenthal, 2001). Total sales in mainstream retail stores in 2000 in the U.S. were over $43 million, ranking saw palmetto sixth in total herb sales (Blumenthal, 2001). In Europe saw palmetto extract is the most commonly used phytotherapeutic agent for benign prostatic hyperplasia (BPH) (Di Silverio *et al.*, 1993), and in Germany it is one of the most frequently prescribed botanical preparations (Blumenthal *et al.*, 1998). Saw palmetto berry was commonly recommended for various prostatic conditions by healthcare professionals in the early part of the 20th century. It was an official drug, listed in the *United States Pharmacopeia* (USP) from 1906 to 1916 and in the *National Formulary* (NF) from 1926 to 1950 (Boyle, 1991) before its use as a therapeutic option for urinary tract disorders by the medical community declined in the U.S. (Tyler, 1994). In the 20th century, the *United States Dispensatory*, 23rd edition, included saw palmetto with an indication for treatment of enlargement of the prostate gland (Wood and Osol, 1943).

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Description

Saw palmetto preparations consist of the berry (fruit) of *Serenoa repens* (W. Bartram) Small (syn. *Sabal serrulata*) [Fam. *Arecaceae*] or its extracts.

Primary Uses

Prostate

Benign prostatic hyperplasia (BPH) (Marks *et al.*, 2001, 2000; Ziegler, 1998; Redecker, 1998; Di Silverio *et al.*, 1998; Braeckman *et al.*, 1997; Bach and Ebeling, 1996; Kondás *et al.*, 1996; Carraro *et al.*, 1996; Braeckman, 1994; Casarosa *et al.*, 1988; Champault *et al.*, 1984). The German Commission E approved the use of saw palmetto for mild to moderate BPH stages I and II (Blumenthal *et al.*, 1998).

Dosage

Internal

Crude Preparations

CUT FRUIT AND OTHER EQUIVALENT GALENICAL PREPARATIONS: 1–2 g (Blumenthal *et al.*, 1998).

CRUDE BERRIES: 10 g twice daily (Pizzorno and Murray, 1999).

FLUID EXTRACT: 1:1 (*g/ml*), 1–2 ml twice daily; 1:2 (*g/ml*) 2–4 ml twice daily (Blumenthal *et al.,* 2000).

SOFT NATIVE EXTRACT: 10:1–14:1 *(w/w*), contains approximately 85–95% fatty acids, 160 mg twice daily (Blumenthal *et al.,* 2000) or 320 mg once daily (Braeckman *et al.,* 1997).

DRY NORMALIZED EXTRACT: 4:1 (*w/w)* contains approximately 25% fatty acids, 400 mg twice daily (Blumenthal *et al.,* 2000).

TEA: Not effective because the lipophilic-active constituents are insoluble in water (Bratman and Kroll, 1999).

NOTE: Most clinical trials have been conducted with native extract.

Duration of Administration

Research suggests that, four to six weeks of treatment are needed for a therapeutic effect (Braeckman, 1994; Champault *et al.*, 1984).

Chemistry

The main constituents of saw palmetto include carbohydrates (inert sugar, mannitol, high-molecular-weight polysaccharides with galactose, arabinose, and uronic acid), fixed oils (free fatty acids and their glycerides), steroids, flavonoids, resin, pigment, tannin, and volatile oil (Newall *et al.*, 1996). The fruits and seeds are rich in triacylglycerol-containing oil (50% of the fatty acids contain 14 or less carbons) (Bruneton, 1999). The liposterolic fraction is the primary active component. A recent systematic review described the chemistry of saw palmetto fruit and related species at different dates of maturity, dosage forms and commercial products, and fruit samples from other species of palm in order to help control the quality of commercial products (Peng *et al.*, 2002).

Pharmacological Actions

Human

Anti-estrogenic activity (Di Silverio *et al.,* 1992); increases urinary flow rate (Redecker, 1998; Ziegler and Holscher, 1998; Braeckman *et al.*, 1997); decreases residual urine (Redecker, 1998; Ziegler and Holscher, 1998; Braeckman *et al.,* 1997); decreases painful urination (Champault *et al.*, 1984); decreases nocturia (Boyle *et al.,* 2000; Ziegler and Holscher, 1998; Vahlensieck *et al.*, 1993a, 1993b); anti-inflammatory (Ziegler and Holscher, 1998); anti-exudative (Ziegler and Holscher, 1998).

Animal

Anti-androgenic in rats (Carilla *et al.,* 1984); relaxes smooth muscle in rats (Gutierrez *et al.,* 1996); anti-edemic (Stenger *et al.,* 1982).

In vitro

Anti-inflammatory (Breu *et al.,* 1992).

Mechanism of Action

Human

- Lowers DHT levels in prostate tissue (Marks *et al.*, 2001).

Animal

- Suppresses prostatic epithelium through a nonhormonal mechanism (Epstein *et al.*, 1999).
- Reduces dihydrotestosterone (DHT) in prostate tissue, which has been implicated as a causative factor of BPH *in vivo* (Koch and Biber; 1994).
- Competes with endogenous estrogen for receptor sites (Di Silverio *et al.*, 1992).
- Induces apoptosis and inhibits cell proliferation in prostate epithelium and stroma (Vacherot *et al.*, 2000).

In vitro

The following mechanisms are based on results from *in vitro* studies using supraphysiologic dosages.

- Inhibits action of 5α-reductase, which catalyzes the metabolism of testosterone to DHT (Bayne *et al.*, 2000; Chavez and Chavez, 1998; Marks *et al.*, 2000; Sultan *et al.*, 1984), due to the free fatty acid content of the fruit's lipophilic extracts (Niederprüm *et al.,* 1994; Weisser *et al.*, 1996).
- Inhibits receptor binding of androgens (Chavez and Chavez, 1998; Sultan *et al.*, 1984).
- Inhibits noncompetitively human α1-adrenoreceptors *in vitro* (Goepel *et al.*, 1999).
- Inhibits both the cyclooxygenase and lipoxygenase pathways *in vitro* (Breu *et al.*, 1992).
- Inhibits growth factors *in vitro* (Plosker and Brogden, 1996).
- Binds selectively to and increases apoptic index for prostate cells *in vitro* (Bayne *et al.,* 2000).

Contraindications

Saw palmetto is not indicated for advanced BPH with severe urinary retention. It should not be used without first ruling out prostate cancer (Bratman and Kroll, 1999). For this reason, the German Commission E clarifies that saw palmetto relieves only the symptoms associated with BPH and recommends consulting a healthcare provider at regular intervals (Blumenthal *et al.*, 1998).

Pregnancy and Lactation: No known restrictions (Blumenthal *et al.,* 2000), although saw palmetto is seldom used by women. Due to potential hormonal activity, saw palmetto is not recommended for pregnant or lactating women, though this has not been confirmed by scientific studies (Blumenthal and Riggins, 1997; Newall *et al.,* 1996; Elghamry and Hänsel, 1969).

Adverse Effects

Rare cases of gastrointestinal disturbance have been reported (Blumenthal *et al.,* 1998). Ingestion on an empty stomach may cause nausea (Bruneton, 1999). Hypertension was reported in 3.1% of patients taking the saw palmetto extract Permixon® (a proprietary form of saw palmetto) (Carraro *et al.*, 1996), although hypertension is not a generally reported effect associated with the use of saw palmetto, either from clinical trials or case reports. The general safety profile of saw palmetto extracts has been shown to be better than finasteride (Wilt *et al.*, 1998). Sexual dysfunction was less common with saw palmetto ($p<0.001$), and the herb has not been associated with erectile dysfunction, ejaculatory disturbance, or altered libido (Wilt *et al.*, 1998). Gastrointestinal disturbances, urinary tract infections, ejaculation problems, and impotence were reported in 2% of patients taking saw palmetto in a clinical trial on 315 men with BPH stage II or III over three years (Brach and Ebeling, 1996). Other trials have noted mild GI upset in a small percentage (1.3%) of patients (Wilt *et al.*, 1998).

Drug Interactions

There are no known interactions associated with saw palmetto (Brinker, 2001). Most clinical trials excluded men taking diuretics, alpha blockers, and anticoagulants; thus, the potential for drug-herb interactions cannot be dismissed, though none have been reported by patients or healthcare providers. A review of the literature does not reveal evidence of adverse drug interactions between saw palmetto and conventional drugs. *In vitro*, saw palmetto potentially inhibits the binding of α1-adrenoceptor antagonists (e.g., tamsulosin and prozacin) and calcium mobilization; the clinical relevance has not been confirmed (Brinker, 2001).

American Herbal Products Association (AHPA) Safety Rating

Class 1: Herbs that can be safely consumed when used appropriately. The editors note that rare cases of stomach problems have been recorded and that the German Commission E suggests regular consultation with a healthcare provider when using saw palmetto for treatment of enlarged prostate, based on the assumption that it treats only the symptoms without eliminating hypertrophic concern (McGuffin *et al.*, 1997).

Regulatory Status

Canada: Approved active ingredient in over 45 licensed products including some Traditional Herbal Medicines (THMs). Natural Health Products (NHPs) and homeopathic medicines (Health Canada, 2002).

France: Authorized as a prescription drug reimbursable by the national health insurance (Chauvarie, 2001).

Germany: Dried fruit and other galenical preparations or lipophilic extracts are approved by the Commission E as nonprescription drugs (Blumenthal *et al.*, 1998). Fresh ripe fruit for preparation of mother tincture and liquid dilutions are official in *German Homeopathic Pharmacopoeia* (GHP, 1993).

BELGIUM: Approved as a prescription adjuvant in BPH treatment.

ITALY: Authorized as a registered drug only (Ris, 2001).

SWEDEN: Classified as Natural Remedy for self-medication requiring premarketing authorization. Two combination products, Curbicin® with pumpkin seed (*Curcubita pepo*) and Prostakan® with nettle root (*Urtica dioica*), are registered in the Medical Products Agency (MPA) "Authorised Natural Remedies" with the approved indication: "Traditionally used in case of micturition problems caused by benign prostatic hyperplasia, e.g. frequent need to urinate and nocturia. Prior to treatment other serious conditions should have been ruled out by doctor" (MPA, 2001). A product monograph for Curbicin® and a document discussing the risk for an anticoagulation effect are included (MPA, 2000, 1999).

SWITZERLAND: Herbal medicine with positive classification (List D) by the *Interkantonale Konstrollstelle für Heilmittel* (IKS) and corresponding sales Category D with sale limited to pharmacies and drugstores, without prescription (Morant and Rupanner, 2001; Ruppanner and Schaefer, 2000). Three saw palmetto monopreparation phytomedicines, six polypreparations (i.e., multi-ingredient products), and 12 saw palmetto homeopathic preparations are listed in the *Swiss Codex 2000/01* (Ruppanner and Schaefer, 2000).

U.K.: Herbal Medicine on the *General Sale List*, Table A (internal or external use), Schedule 1 (requires full Product License) (MCA, 2002).

U.S.: Dietary supplement (USC, 1994). In view of the levels of evidence in clinical trials of "moderate scientific quality" indicating that commercial extracts of saw palmetto are more effective than placebo to treat symptoms of BPH, the *United States Pharmacopeia* (USP) moved saw palmetto preparations from *National Formulary* (NF) status to inclusion into the USP. This is the first time this has been done for an herb formerly classed only as a dietary supplement. This USP status is designated only for articles that are either approved by the Food and Drug Administration and/or have a USP-accepted use (USP, 2002). The mother tincture 1:10 (*w/v*), 65% alcohol (*v/v*), of ripe fruit, is an OTC Class C drug official in *Homeopathic Pharmacopoeia of the United States* (HPUS, 1992).

Clinical Review

Nineteen studies are outlined in the following table, "Clinical Studies on Saw Palmetto," including 7,210 participants. All but two (Gerber *et al.*, 1998; Champault *et al.*, 1984), demonstrated positive effects for BPH. Numerous studies concluded that saw palmetto improves symptoms of BPH including one randomized, single-blind, placebo controlled, parallel group multi-center study (R, SB, PC, PG, MC) (Braeckman *et al.*, 1997), two open-label (OL), MC studies, (Braeckman, 1994; Ziegler and Holscher, 1998), an R, DB, controlled study (Carraro *et al.*, 1996), a R, comparative study (Di Silverio *et al.*, 1998), a prospective MC study (Bach and Ebeling, 1996), a R, PC study (Champault *et al.*, 1984), and two observational studies (Vahlensieck *et al.*, 1993a and 1993b). Two OL studies found positive results (Kondás *et al.*, 1996; Redecker, 1998), but another OL study failed to find significant improvement in objective measures of bladder outlet obstruction (Gerber *et al.*, 1998). Similarly, one DB, C study found no difference between saw palmetto and placebo (Reece *et al.*, 1986). Several clinical trials (Carraro *et al.*, 1996; Rhodes *et al*, 1993; Strauch *et al.*, 1994) have shown that serum levels of testosterone, dihydrotestosterone, and prostate-specific-antigen (PSA) are not changed significantly. One PC study looked at hormone levels, finding no changes in testosterone, luteinizing hormone (LH), or follicle stimulating hormone (FSH) levels (Casarosa *et al.*, 1988).

It is well-accepted that at least 30–50% of BPH patients report an improvement in their symptoms after treatment with placebo (Bruneton, 1999). This percentage is about the same after simple monitoring (Chapple, 1993). Two meta-analyses of 18 R, PC trials concluded that saw palmetto treatment for at least 30 days improves urologic symptoms and flow measures (Wilt *et al.,* 1998*,* 2000). Adverse effects were mild and infrequent. The authors concluded that further research is needed using standardized preparations to determine saw palmetto's long-term effectiveness and ability to prevent BPH complications. Another meta-analysis (Boyle *et al.*, 2000) focused on 11 R clinical trials and two OL trials using saw palmetto extract on men with BPH. The analysis concluded that saw palmetto compared to placebo provided significant improvement in the peak urinary flow rate and a reduction in nocturia.

Some anecdotal reports state that saw palmetto can mask prostate cancer by lowering PSA levels. However, several large studies including a total of 1,256 patients did not show this effect (Carraro *et al.*, 1996; Braeckman, 1994). Originally, it was thought that saw palmetto relieves the symptoms associated with an enlarged prostate without reducing the enlargement (Blumenthal *et al.*, 1998). However, a recent study has detected shrinkage of the epithelial tissue in the transition zone of the gland (Marks *et al.,* 2000; Marks and Tyler, 1999). Further studies are needed to confirm the finding.

A meta-analysis of recent PC trials included seven clinical studies (Boyle *et al.*, 2000). All trials lasted three months, and indicated a decrease in nocturia frequency (0.5 times per night) and an increase in the peak rate of urinary flow rate by 1.5 ml/second over placebo. A six-month, R, DB, PC study (Carraro *et al.*, 1996) comparing Permixon® and finasteride (Proscar®) included 951 patients with BPH, and showed an equally improved symptom score in both groups (37% with Permixon® vs. 39% with finasteride), and equally improved peak urinary flow rates. One of the first U.S. trials (Gerber *et al.*, 1998) reported symptomatic, but not urodynamic, improvement in 46 men treated for six months with a saw palmetto berry extract.

Five studies focused on a saw palmetto and nettle combination for BPH symptoms. One R, DB, PC study on the Nutralite® product examined use of a saw palmetto, nettles, lemon bioflavonoid extract, and vitamin A combination, and found significant improvement in prostate epithelial contraction without adverse effects (Marks *et al.*, 2000). The same combination produced a 32% reduction in dihydrotestosterone levels compared to baseline in six months in prostate tissue extracted via needle biopsy (Marks *et al.,* 2001). Four well-designed studies on the fixed combination, PRO 160/120®, ranging from 12 weeks to one year, found good efficacy and tolerance (Sökeland, 2000; Sökeland and Albrecht, 1997; Metzher *et al.*, 1996; Schneider *et al.*, 1995).

Branded Products*

IDS 89: Strathmann AG & Co. / Sellhpsweg 1 / 22459 / Hamburg / Germany / Tel: +49-401-55-9050 / Fax: +49-40-55-9051-00 / www.strathmann.de / Email: info@strathmann.de.

LG 166/S: Laboratori Guidotti S.p.A, Via Trieste 40 56126 Pisa, Italy / Tel: +39-05-05-0521-1 / Fax: +39-05-04-0250 / Email: a.viti@giofil.it / www.giofil.it. 160 mg liposterolic extract.

Nutrilite® Saw Palmetto with Nettle Root: Nutrilite® / 5600 Beach Blvd. / Buena Park, CA 90622 / U.S.A. / Tel: (714) 562-6200 / www.nutrilite.com. One tablet contains 106 mg saw palmetto lipoidal extract and 80 mg nettle root extract.

Permixon®: Pierre Fabre Médicament / 45, Place Abel-Gance / 92654 Boulogne / France / Tel: +33-01-49-10-8000 / Fax: +33-01-49-10-9712 / www.dermaweb.com. Liposterolic hexane extract of saw palmetto berries, comprised of free (90%) and esterified (7%) fatty acids, sterols, polyprenic compounds, and flavonoids. This extract was the template for current liposterolic extracts manufactured using either ethanol or carbon dioxide extraction.

PRO 160/120®: Dr. Willmar Schwabe Pharmaceuticals / International Division / Willmar Schwabe Str. 4 / D-76227, Karlsruhe / Germany / Tel: +49-721-4005 ext. 294 / www.schwabepharma.com / Email: melville-eaves@schwabe.de. Fixed combination of 160 mg of saw palmetto extract (WS 1473), 10–14.3:1, and 120 mg of stinging nettle root (*Urtica dioica*) dry extract (WS 1031), 8.3–12.5:1.

Prostagutt® (a.k.a. WS 1473): Dr. Wilmar Schwabe Pharmaceuticals. Liposterolic extract made from alcohol extraction.

Prostagutt® forte: Dr. Willmar Schwabe Pharmaceuticals. Fixed combination of 160 mg of saw palmetto extract (WS 1473), 10–14.3:1, and 120 mg of stinging nettle root (*Urtica dioica*) dry extract (WS 1031), 8.3–12.5:1.

Prostaserene®: Therabel Research / Egide Van Ophemstraat 110 / 1180 / Bruxelles / Belgium / Tel: +32-02-370-4611 / Fax: +32-02-370-4690. Liposterolic extract of saw palmetto berries.

Solaray® Saw Palmetto: Nutraceutical Corporation / 1400 Kearns Blvd / Park City, Utah 84060 / U.S.A. / Tel: 800-669-8877 / www.nutraceutical.com. Each 160-mg gelcap contains 85%-95% (approximately 136 mg) essential fatty acids and steroids.

Strogen forte®: Strathmann AG & Co. The liposterolic extract is produced through carbon dioxide extraction. Sabal extract IDS 89 is a constituent of Strogen® forte.

Strogen® S: Strathmann AG & Co. Sabal extract IDS 89 is a constituent of Strogen® S.

Talso®: Sanofi Synthelabo GmbH / 174 avenue de France / 75013 Paris / France / Tel: +331 53 77 4000 / www.sanofi-synthelabo.fr.

*American equivalents, if any, are found in the Product Table beginning on page 398.

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Clinical Studies on Saw Palmetto (*Serenoa repens* [W. Bartram] Small)

Benign Prostatic Hyperplasia (BPH)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Ziegler and Holscher, 1998	BPH	O, MC n=109 men with BPH in Stages I and II	3 months	160 mg; 2x/day	Prostagutt® (WS 1473)	Saw palmetto caused a significant ($p<0.001$) improvement in subjective assessment. Therapy was well-tolerated. Significant improvement in mean flow rate ($p<0.0001$), micturition time ($p<0.0001$), and time to peak flow rate ($p<0.0001$) with intent-to-treat analysis. No significant change in micturition volume. Significant decrease in residual volume ($p<0.0001$), significant decline in daytime micturition ($p<0.0001$) and in nocturia ($p<0.0001$).
Redecker, 1998	BPH	O n=50 men with BPH in Stages I and II	3 months	160 mg; 2x/day	Prostagutt® (WS 1473)	Saw palmetto caused a significant increase in maximum urinary flow rate ($p<0.001$), a reduction in residual urine volume, and reduction of micturition frequency (26 ml to 15 ml).
Di Silverio, 1998	BPH	R, C n=25 men with BPH	3 months	160 mg; 2x/day or no treatment	Permixon®	Compared to control, those receiving saw palmetto had a significant reduction in prostatic DHT ($p<0.001$) and epidermal growth factor (EGF) ($p<0.01$). They had a significant increase in testosterone levels ($p<0.001$). Highest values were in peri-urethral area.
Braeckman, 1997	BPH	R, SB, PC, P MC n=132 men with BPH	1 year	160 mg; 2x/day, or 320 mg, 1x/day	Prostaserene®	Both doses of saw palmetto extract significantly improved International Prostate Symptom Score ($p<0.0001$), quality of life score ($p<0.0001$), prostatic volume ($p<0.0001$), maximum flow rate ($p<0.0001$), mean flow rate ($p<0.01$), and residual urinary volume. The two doses were not significantly different. The extract was found to be safe.
Bach and Ebeling, 1996	BPH	P, MC n=315 men with BPH Stage II or III	3 years	160 mg; 2x/day	Strogen® S (IDS 89)	For 80% of patients, clinical status and quality of life improved markedly. 50% of patients had an improvement in residual urine, flow time, and flow rate. Adverse side effects (e.g., gastrointestinal disturbances, urinary tract infections, ejaculation problems, impotence) were experienced by 2% of patients.
Kondás *et al.*, 1996	BPH	O n=38 men with moderate BPH Stages II–III (Vahlensieck)	12 months	320 mg/day	Strogen forte® (IDS 89)	Of patients participating, 74% had an improvement on International Prostate Symptom Score. Greatest improvement rates were noted for sensation of residue, interruption of micturition, and force of urinary stream. Subjective reports of improvement did not depend on size of hyperplastic prostate. Significant increase in average peak flow rate ($p<0.001$). Decrease in residual volume ($p<0.001$). Decrease in average volume of prostate ($p<0.02$). No adverse reactions.
Carraro, 1996	BPH	R, DB, C n=951 men with moderate BPH	6 months	160 mg, 2x/day Permixon® or 5 mg/day finasteride	Permixon® and finasteride	Both treatments equally decreased symptoms of BPH. Saw palmetto had minimal effect on prostate volume and no effect on PSA concentration. Saw palmetto was more effective than finasteride in reducing lower urinary tract symptoms in men with smaller prostate size. Significant results in favor of finasteride for urinary flow rate and prostate volume. Significant decrease in PSA levels with finasteride. Significantly more subjects withdrew from study with finasteride.
Braeckman, 1994	BPH	O, MC n=305 men with mild to moderate BPH	3 months	160 mg, 2x/day	Prostaserene®	After 45 days of treatment there was significant ($p<0.0001$) improvement in International Prostate Symptom Score, quality of life, urinary flow rate, residual urinary volume, and prostate size. Serum PSA concentration was not modified by saw palmetto extract, decreasing the risk of possible development of prostate cancer during treatment. Only 5% of patients reported side effects.

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.

Clinical Studies on Saw Palmetto (*Serenoa repens* [W. Bartram] Small) (cont.)

Benign Prostatic Hyperplasia (BPH) (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Vahlensieck *et al*., 1993a	BPH	OB n=578 (BPH Stages II and III)	8 months; 12 weeks of treatment	160 mg, 2x/day	Talso®	Clear clinical improvements were seen in symptoms, including urine flow, urine retention, nocturia, and daytime micturition. The residue urine volume was reduced by approximately half after 12 weeks, with 30% reduction after 4 weeks. The physicians evaluated efficacy as good or very good in over 80% of the subjects with over 95% of the subjects demonstrating good or very good tolerability.
Vahlensieck *et al*., 1993b	BPH	OB n=1,334	8 months	160 mg, 2x/day	Talso®	The study was based on symptom treatment and patient evaluations. During the treatment period, pollakiuria was reduced by 37%, nocturia by 54%, and the volume of residual urine was reduced by 50%. The number of patients with dysuria was reduced from 75% to 37%. 80% of the patients rated good or very good efficacy at 80% and good or very good tolerability at 95%.
Casarosa, 1988	BPH	PC n=20 men with BPH and normal levels of testosterone, LH, and FSH. (50–70 years)	30 days	160 mg, 2x/day or placebo	LG 166/S	One month of treatment with saw palmetto extract did not alter testoterone, LH, or FSH levels. These findings are in contrast to those of Tenaglia and DiSilverio (1986) who found increases in the hormone levels. The authors have no explanation for the discrepancy.
Champault, 1984	BPH	R, PC n=110 men (ages 47–92), with BPH, not needing surgery	28 days	160 mg, 2x/day or placebo	Saw palmetto extract (PA 109)	Patients taking saw palmetto had significant decrease in nocturnal micturitions ($p<0.001$), dysuria (painful urination), and rate of micturition as compared to placebo. No adverse effects reported. Significant increase in urinary flow with saw palmetto extract ($p<0.001$).

Combination Preparations

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Marks *et al*., 2001	BPH	R, PC, Cm n=40 (saw palmetto vs. placebo), n=22 (finasteride vs. control), measuring prostate tissue androgen levels using needle biopsies	6 months	318 mg saw palmetto extract/day; 1 tablet, 3x/day with meals, or placebo	Nutrilite® Saw Palmetto with Nettle Root (containing saw palmetto extract 106 mg, nettle root extract 80 mg, lemon bioflavonoid extract 33 mg, and vitamin A, 190 IU)	In the saw palmetto group, tissue DHT levels were reduced by 32% from 6.49 ng/g to 4.40 ng/g ($p<0.005$). The effect of chronic finasteride therapy was statistically significant ($p<0.01$) in lowering prostate tissue DHT levels (80%) compared to levels of testosterone. No significant change in tissue DHT levels was observed with the placebo.
Marks *et al*., 2000	BPH	R, DB, PC n=41 men with symptomatic BPH. OL extension after 6 months	6 months	318 mg saw palmetto extract/day, 1 tablet, 3x/day with meals, or placebo	Nutrilite® Saw Palmetto with Nettle Root (containing saw palmetto extract 106 mg, nettle root extract 80 mg, lemon bioflavonoid extract 33 mg, and vitamin A, 190 IU)	Saw palmetto blend group had non-statistically significant improvement vs. placebo in clinical parameters (e.g., International Prostate Symptom Score, uroflowmetry, residual urine volume, prostate volume). After 6 months, saw palmetto blend was associated with prostate epithelial contraction, notably in transition zone ($p<0.01$), suggesting possible mechanism for clinical significance found by other studies. No serious adverse effects were associated with saw palmetto blend.

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Benign Prostatic Hyperplasia (BPH)

Combination Preparations (cont.)

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Sökeland, 2000	BPH	R, MC, DB n=431	48 weeks	2 capsules PRO 160/120®/day vs. finasteride (5 mg/day) vs. placebo	PRO 160/120® (Prostagutt forte™, fixed combination of 160 mg of saw palmetto extract [WS 1473] and 120 mg of stinging nettle dry extract [WS 1031]) or finasteride	The efficacy of both PRO 160/120® and finasteride were shown to be equivalent in the International Prostate Symptom Score with tolerability significantly better with PRO 160/120®. 96 adverse events were recorded in 54 patients using finasteride compared with 74 in 52 patients taking PRO 160/120®.
Sökeland and Albrecht, 1997	BPH (Stages I and II)	R, RC, MC, DB, PG n=543	48 weeks	2 capsules PRO 160/120®/day vs. finasteride (5 mg/day) vs. placebo or one capsule of 5 mg of finasteride per day	PRO 160/120® (Prostagutt forte™, fixed combination of 160 mg of saw palmetto extract [WS 1473] and 120 mg of stinging nettle dry extract [WS 1031]) or finasteride	International-Prostate-Symptom-Score (I-PSS) value improved by a total of 4.8 points with the PRO 160/120®. The study found equivalent efficacy between the two groups. Less adverse events, including diminished ejaculation volume, erectile dysfunction and headache, were reported in the PRO 160/120® group. The study recommended that patients should receive finasteride only after the use of the combination for at least 3 months was unsuccessful.
Metzker *et al.*, 1996	BPH (Stages I and II)	DB, PC n=40	350 days	2 capsules PRO 160/120®/day vs. finasteride (5 mg/day) vs. placebo	Prostagutt forte™ (fixed combination of 160 mg of saw palmetto extract [WS 1473] and 120 mg of stinging nettle dry extract [WS 1031])	The study concluded good efficacy and tolerance in the administration of PRO 160/120® for approximately one year of therapy. After 24 weeks, maximum urine volume per second by 3.3 ml/s had occurred with the combination compared to only a slight improvement of 0.55 ml/s with placebo. Subjective reports corresponding to the I-PSS found a highly significant ($p<0.001$) advantage with the combination vs. placebo.
Schneider *et al.*, 1995	BPH (Stages I and II)	S n=2,080	12 weeks	2 capsules PRO 160/120®/day vs. finasteride (5 mg/day) vs. placebo	Prostagutt forte™ (fixed combination of 160 mg of saw palmetto extract [WS 1473] and 120 mg of stinging nettle dry extract [WS 1031])	Treatment with the combination was found to be an effective method to avoid surgery or not to make it necessary as soon. Physician and patient assessment confirmed the efficacy and tolerance of PRO 160/120®.

Lower Urinary Tract Symptoms

Author/Year	Subject	Design	Duration	Dosage	Preparation	Results/Conclusion
Gerber *et al.*, 1998	Lower urinary tract symptoms	O n=46 men with lower urinary tract symptoms secondary to BPH	6 months	160 mg, 2x/day	Solaray® Saw Palmetto	The International Prostate Symptom Score significantly improved ($p<0.001$) after 2 months of treatment. No significant change in peak urinary flow rate, post void residual urine volume, or detrusor pressure at peak flow. No significant improvement in objective measures of bladder outlet obstruction. Saw palmetto was well-tolerated.

KEY: C – controlled, **CC** – case-control, **CH** – cohort, **CI** – confidence interval, **Cm** – comparison, **CO** – crossover, **CS** – cross-sectional, **DB** – double-blind, **E** – epidemiological, **LC** – longitudinal cohort, **MA** – meta-analysis, **MC** – multi-center, **n** – number of patients, **O** – open, **OB** – observational, **OL** – open label, **OR** – odds ratio, **P** – prospective, **PB** – patient-blind, **PC** – placebo-controlled, **PG** – parallel group, **PS** – pilot study, **R** – randomized, **RC** – reference-controlled, **RCS** – retrospective cross-sectional, **RS** - retrospective, **S** – surveillance, **SB** – single-blind, **SC** – single-center, **U** – uncontrolled, **UP** – unpublished, **VC** – vehicle-controlled.