

# ***Serenoa repens***



*Serenoa repens* (Saw Palmetto) Indena photos

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### **Description**

*Serenoa repens* (also known as *Sabal serrulata*, Saw Palmetto or Dwarf palm) is native to the U. S. South Atlantic coast, as well as Southern Europe and North Africa. This small palm tree grows to a height of six to ten feet, and has a fan-shaped crown of leaves and dark red berries approximately the size of olives.

Traditional indications for the use of Saw palmetto include cystitis, chronic bronchitis, asthma, diabetes, dysentery, indigestion, and “underdeveloped breasts.” The berries have also been thought to be an aphrodisiac.<sup>1</sup> Modern usage of Saw palmetto is overwhelmingly for the treatment of benign prostatic hyperplasia (BPH).

### **Active Constituents**

The berries contain approximately 1.5 percent volatile oil, comprised of 63 percent free fatty acids and 37 percent ethyl esters of those fatty acids. The fatty acids include caproic, caprylic, capric, lauric, palmitic, and oleic acids, and ethyl esters of these. In addition, the berries contain beta-sitosterol and its glucoside, beta sitosterol D-glucoside, as well as ferulic acid.<sup>1</sup> Myristoleic acid has recently been identified as a cytotoxic component in *Serenoa repens* extract, which raises the possibility that usage of Saw palmetto may be extended to the treatment of prostatic cancer.<sup>2</sup>

### **Mechanisms of Action**

Testosterone is converted in prostatic cells to dihydrotestosterone (DHT), catalyzed by the enzyme steroid 5-alpha-reductase (5-AR). DHT binds to androgen receptors in the nucleus of prostate cells, stimulating cellular growth and division.<sup>3-5</sup> In benign prostatic hyperplasia (BPH) tissue, 5-AR levels are higher than in tissue not affected by BPH.<sup>4,5</sup> The presence of

DHT may also stimulate 5-AR activity, causing a positive feedback loop, and more DHT.<sup>6</sup> The standardized liposterolic Serenoa extract has been found to be a potent inhibitor of 5-AR, resulting in decreased tissue DHT. Serenoa also competitively inhibits binding of testosterone and DHT to cytosolic and nuclear androgen receptors.<sup>7-9</sup> As a 5-alpha-reductase inhibitor, the liposterolic extract of *Serenoa repens* demonstrates selectivity and specificity to prostatic cells when compared to epididymis, testes, kidney, skin, and breast cells.<sup>10</sup>

Another component of BPH is inflammation within the prostate gland. A standardized Serenoa extract has been shown to inhibit 5-lipoxygenase, and thus the downstream pro-inflammatory arachidonic acid metabolites leukotriene B4 (LTB4) and 5-hydroxyeicosatetraenoic acid (5-HETE).<sup>11</sup>

## **Clinical Indications**

### ***Benign Prostatic Hyperplasia***

The liposterolic extract of the fruit, standardized to contain at least 85 percent fatty acids and sterols, is currently used in the treatment of BPH. Benign prostatic hyperplasia is one of the most common medical conditions in middle-aged and elderly males, with an incidence of 50-60 percent in men ages 40-60, and greater than 90 percent in men over 80. The disease process leading to symptomatology in older males probably begins as early as the late 20s, and may have an incidence rate of 10 percent at that age. Rarely a fatal disease, BPH affects lifestyle and comfort.<sup>12</sup>

A non-malignant hypertrophy of the prostate caused by hormonal processes and/or imbalances within the prostate, BPH begins in the periurethral region and includes the stromal, epithelial, and smooth muscle tissues of the gland. The fibrous capsule surrounding the gland forces most of the growth inward, compressing the urethra and causing the typical urinary symptoms characteristic of the disease. Primary symptoms include decreased force and caliber of the urine stream; urinary hesitancy, urgency, and frequency; post-void dribbling; incomplete emptying of the bladder; dysuria; and nocturia.<sup>12</sup>

In a double-blind, placebo-controlled study of 110 BPH patients, 160 mg twice per day of a standardized Serenoa extract significantly improved nocturia, dysuria, post-voiding residual urine, flow rate, patient self-rating, and the physician's overall assessment.<sup>13</sup> In another double-blind clinical study, urinary symptoms and flow rates were significantly improved in 42.9 percent of patients taking a Serenoa extract, compared to 15.4 percent of patients given placebo.<sup>14</sup> In an open trial, 67 percent of patients on Serenoa described their subjective symptom relief as "excellent," while 25 percent characterized their relief as "good."<sup>15</sup> No side effects or toxicity were noted.

An impressive review of randomized trials found via MEDLINE (1966 to 1997 search) compared treatment results of six phytotherapeutic agents: *Serenoa repens*, *Hypoxis rooperi*, *Secale cereale*, *Pygeum africanum*, *Urtica dioica*, and *Cucurbita pepo*. Studies were included

if men had BPH symptoms, phytotherapeutic agents were used singularly or in combination, a control group received placebo or pharmaceutical therapy for BPH, and treatment duration was a minimum of 30 days. This comprehensive study concluded that, when compared to the other phytotherapies, *Serenoa repens* provided the strongest therapeutic evidence for BPH.<sup>16</sup> Unlike other 5-alpha-reductase inhibitors, *Serenoa repens* creates this effect without inhibition of cellular prostate specific antigen (PSA) secretion. This allows for the continued use of PSA values for prostate cancer screening.<sup>17</sup>

The standard pharmaceutical therapy for BPH is the drug Proscar® (finasteride), a 5-AR inhibitor. A six-month, double-blind study of 1,098 BPH patients over 50 years of age compared Proscar (5 mg per day) with a standardized Serenoa extract (160 mg twice per day). Both treatments decreased BPH symptoms equally and improved quality of life. Although both treatments significantly improved symptomatology, it is interesting to note Proscar reduced prostate size by 18 percent and the Serenoa extract reduced it six percent.<sup>18</sup>

## **Prostate Cancer**

*In vitro* studies have also demonstrated that myristoleic acid, found in the extract of *Serenoa repens*, induces apoptosis and necrosis in prostatic tumor cells,<sup>2,19</sup> posing the potential for Serenoa in the prevention and treatment of prostate cancer.

## **Polycystic Ovary Syndrome (PCOS)**

Because of its antiandrogenic effects, Serenoa has been used clinically for polycystic ovary syndrome. Although formal studies have not been conducted to confirm the efficacy of Serenoa in PCOS, anecdotal clinical evidence points to its use in a protocol for this condition.<sup>20</sup>

## **Side Effects and Toxicity**

There are no known cases of toxicity. Occasionally patients experience minor gastrointestinal symptoms including nausea and/or abdominal pain.<sup>21</sup>

## **Dosage**

The dose of the standardized liposterolic Serenoa extract (85-95% fatty acids and sterols) used in the majority of clinical studies on BPH is 160 mg twice per day. Clinical results may be seen in six to eight weeks, although a six-month trial is the minimum to assess clinical efficacy. A three-month, double-blind comparison study of two dosage regimens – 160 mg once daily versus 160 mg twice daily – showed no significant differences between the dosages. This study of 100 outpatients with BPH symptoms noted improvements in maximum and mean urinary flow rates as well as a decrease in residual urine volume. Both dosage regimens significantly reduced the International Prostate Symptom Score (I-PSS) mean total compared to patient baseline.<sup>22</sup>

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