

# Prostate SAP

Science-based support for prostate health\*

The average male will experience a concern with their prostate at some point during their lifetime.\* The condition known as benign prostatic hypertrophy (BPH) becomes increasingly prevalent in men as they age, with 50% of men experiencing BPH by the age of 60, and 90% of men by the age of 85.\*<sup>[1]</sup> This condition can cause a multitude of symptoms, including difficulty starting the flow of urine, discomfort with urination, and increased risk of urinary tract infections due to urine stagnation in the bladder, which may potentially lead to kidney damage.\*<sup>[2]</sup> BPH can interfere with activities of daily living and have a serious impact in a male's life.\* Several herbs and nutrients have been studied that demonstrate the ability to prevent and treat BPH, and in many cases eliminate symptoms entirely.\*<sup>[3][4]</sup> Prostate cancer will affect 1 in 7 men in their lifetime, and is the most common form of cancer detected in males.\*<sup>[5]</sup>

## SUPPLEMENT FACTS

Serving Size: 2 Softgels

Servings Per Container: 30

	Amount Per Serving	% Daily Value
Vitamin D (as cholecalciferol) (1,000 IU)	25 mcg	125%
Vitamin E (from mixed tocopherol concentrate from non-GMO soy) (12 IU)	8 mg AT	53%
Vitamin B6 (from 20 mg pyridoxine hydrochloride)	16.5 mg	968%
Zinc (from zinc citrate)	32 mg	291%
Selenium (from yeast-free L-selenomethionine)	100 mcg	182%
Free plant sterols (from non-GMO soy) (148 mg beta-sitosterol, 74 mg stigmasterol, and 74 mg campesterol)	370 mg	**
Extra virgin olive oil	350 mg	**
Wild-crafted saw palmetto ( <i>Serenoa repens</i> ) fruit	320 mg	**
Rye ( <i>Secale cereale</i> ) flower pollen extract	210 mg	**
Borage ( <i>Borago officinalis</i> ) seed oil	200 mg	**
Pumpkin ( <i>Cucurbita pepo</i> ) seed oil, cold-pressed	200 mg	**
L-Alanine	100 mg	**
Cranberry ( <i>Vaccinium macrocarpon</i> ) fruit concentrate	100 mg	**
L-Glutamic acid hydrochloride	100 mg	**
Glycine	100 mg	**
Stinging nettle ( <i>Urtica dioica</i> ) root and herb top extract, 5% silicic acid	50 mg	**
Pau d'arco ( <i>Tabebuia heptaphylla</i> ) inner bark	30 mg	**
Lycopene (from tomato [ <i>Solanum lycopersicum</i> ] flesh)	1.2 mg	**

\*\*Daily Value not established

**Other ingredients:** Lecithin (from non-GMO sunflower); medium-chain triglycerides (MCT) oil; silicon dioxide; and beeswax in a softgel composed of annatto (in sunflower oil), bovine gelatin, glycerin, and purified water.

**This product is non-GMO.**

**Contains no:** Gluten, wheat, eggs, dairy, yeast, citrus, preservatives, artificial flavor or color, or added sugar.

**Store in a tightly closed, light-resistant container in a cool, dry place.**

## DIRECTIONS FOR USE

**Adult men:** Take 2 softgels daily with food or as directed by your healthcare practitioner. If you are taking other medications, take this product a few hours before or after them.

**Duration of use:** Consult a healthcare practitioner for use beyond 4 months.

## INDICATIONS

### Prostate SAP:

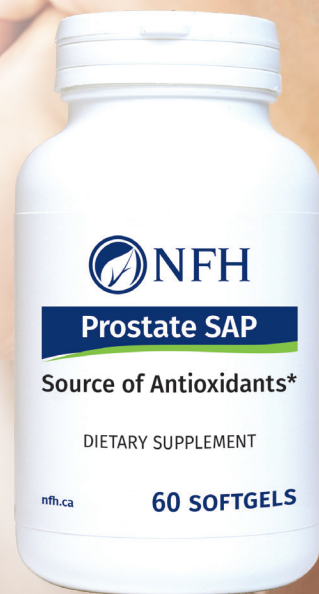
- Is targeted as treatment and preventative therapy for any male over the age of 40 to help maintain a healthy prostate and urinary tract system.\*
- Can be used to help reduce benign prostatic hypertrophy.\*
- May also be protective against the development of prostate cancer.\*<sup>[6]</sup>

## PURITY AND STABILITY

All ingredients listed for all **Prostate SAP** lot numbers have been tested by a third-party laboratory for identity, potency, and purity.

\* These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

Scientific Advisory Panel (SAP):  
adding nutraceutical research  
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Lower urinary tract symptoms, benign prostate hypertrophy (BPH), bladder outlet obstruction, and prostate cancer have become increasingly common in the aging male population.<sup>[7]</sup> BPH affects more than 90% of men by the time they reach 90 years of age.<sup>[1]</sup> The precise cause of BPH has not yet been determined, but inflammation does play a pivotal role and is the target of many pharmaceuticals designed to treat BPH.<sup>[3]</sup> Growth of the prostate gland is controlled by the endocrine system, but the precise way each hormone affects the prostate gland is not well understood. During puberty, testosterone is thought to act to enlarge the prostate, but as men age their testosterone levels decline, and this is when the prostate growth often becomes problematic. There is some thought that the ratio between free testosterone and estrogen contributes to prostate enlargement, but this has not to date been demonstrated in the literature. There are several natural compounds that have demonstrated the ability to reduce symptoms caused by BPH.

#### SAW PALMETTO (*Serenoa repens*)

Saw palmetto is one of the most common herbs used for the treatment of lower urinary tract symptoms in males due to BPH. Researchers have determined that saw palmetto has several different mechanisms of action including the inhibition of 5 $\alpha$ reductase, as well as antiandrogenic, antiproliferative and anti-inflammatory effects.<sup>[4]</sup> Two active components of saw palmetto are oleic and lauric acids: It has been demonstrated that they bind to  $\alpha$ 1 adrenergic, muscarinic and 1,4-DHP receptors, and have the ability to inhibit 5 $\alpha$ reductase.<sup>[4]</sup> These mechanisms may lead to the therapeutic effect seen in cases of BPH that result in fewer urinary-tract symptoms.<sup>[4]</sup>

A review article exploring the efficacy of saw palmetto compared to placebo for urinary tract symptoms in men found that there was a statistically significant improvement in urinary flow and urinary symptom scores in subjects using saw palmetto.<sup>[8]</sup> Researchers concluded that saw palmetto was a well-tolerated treatment that provided mild to moderate improvement in urinary symptoms and flow.<sup>[8]</sup> The efficacy of saw palmetto was also compared to finasteride, a commonly prescribed pharmaceutical for BPH, and was found to have similar improvements in urinary symptom scores, with fewer adverse effects.<sup>[8]</sup>

Research has also been conducted exploring the role of saw palmetto in prostate cancer. Saw palmetto has been found to have the ability to selectively induce apoptosis in prostate cancer cells through the intrinsic pathway, via activation of the mitochondrial permeability transition pore.<sup>[9]</sup>

#### PUMPKIN (*Cucurbita pepo*) SEED OIL

A double-blind, placebo-controlled study was performed over a 12-month period with patients who had BPH with an International Prostate Symptom Score (IPSS) over 88. The IPSS measures quality of life, serum prostate-specific antigen (PSA), prostate volume, and maximal urinary flow rate. The groups receiving 320 mg/d pumpkin seed oil (group B), 320 mg/d saw palmetto (group C), or both (group D) all demonstrated an improvement in their score by 3 months.<sup>[10]</sup> Group D was the only group that had a reduction in serum PSA levels after 3 months.<sup>[10]</sup> The results of this trial indicated that pumpkin seed oil and saw palmetto oil are clinically safe and may be an effective treatment for BPH, particularly in combination.<sup>[10]</sup>

#### STINGING NETTLE (*Urtica dioica*)

A double-blind, placebo-controlled study exploring the use of stinging nettle for BPH was conducted using 620 patients.<sup>[11]</sup> Following the 6-month trial, 81% of patients in the stinging nettle group reported an improvement in lower urinary tract symptoms compared to 16% of controls.<sup>[11]</sup> The treatment group had an average improvement in their IPSS from 19.8 to 11.8 compared to a change of 19.2 to 17.7 in the placebo group.<sup>[11]</sup> Peak flow rates improved on average by 8.2 ml/s in the treatment group compared to 3.4 ml/s in the placebo group.<sup>[11]</sup> No change was observed in serum PSA or testosterone in either group. There were also no side effects identified in either group.<sup>[11]</sup> This study's authors concluded that symptomatic BPH could have beneficial effects from treatment with stinging nettle.<sup>[11]</sup>

#### FREE PLANT STEROLS

Plant sterols, or phytosterols, may be beneficial for the treatment of abacterial prostatitis.<sup>[12]</sup> A study found that the proliferation of chronic prostatitis was decreased in the group receiving phytosterols. Researchers found that phytosterols were able to reduce serum levels of IL1 $\beta$  and TNF $\alpha$ , and also reduced the expression of prostate COX2 and SLOX.<sup>[12]</sup> The results demonstrated that phytosterols have a positive therapeutic effect on abacterial prostatitis.<sup>[12]</sup>

#### LYCOPENE

There are several pathways that have been identified as playing a role the development of prostate cancer.<sup>[6]</sup> Free radicals produced from inflammatory processes can potentially lead to oxidative DNA damage, which if unrepaired can become mutagenic.<sup>[6]</sup> The cytokines IL6 and IL4, as well as growth factor signaling pathways, have all been identified as contributors to prostate growth.<sup>[6]</sup> Lycopene modulates several of these pathways: it can reduce inflammatory signals, prevent oxidative damage and modulate the activity of androgen signaling and the growth factor axis. These are likely the mechanisms that result in cell growth inhibition and apoptosis that are seen with the use of lycopene.<sup>[6]</sup>

#### ZINC CITRATE

The prostate gland usually contains a high concentration of zinc; however, levels are dramatically reduced in cases of prostate cancer.<sup>[13]</sup> Researchers explored the antiproliferative effects of zinc in BPH cells as well as in prostate cancer cells.<sup>[13]</sup> Both prostate cancer cells and BPH cells were treated with zinc and cell growth, viability and apoptosis were examined.<sup>[13]</sup> The BPH cells were found to be more sensitive to the antiproliferative effects of zinc when compared to the prostate cancer cells.<sup>[13]</sup> The variation in response to zinc in the prostate cancer and BPH cells does suggest that zinc may play an important role in the regulation of both cell growth and apoptosis in hyperplastic and prostate cancer cells.<sup>[13]</sup>

#### SELENIUM AND VITAMIN E

Selenium can play an important role in prostate health, as it helps to maximize the activity of glutathione peroxidase and is a powerful antioxidant in the body.<sup>[14]</sup> A trial using healthy middle-aged men taking 200  $\mu$ g of selenium for 6 weeks found that supplementation raised the activity of both erythrocyte and plasma glutathione peroxidase, and lowered values of plasma prostate-specific antigen.<sup>[14]</sup> This effect was not seen in the placebo treatment group. The study indicates that the average male in the US does not consume an adequate amount of selenium in their diet.<sup>[14]</sup> In a separate study, researchers looked at a deficiency of trace elements and the link to PSA values.<sup>[15]</sup> Results showed that serum selenium, zinc and vitamin E were significantly lower in the prostate cancer patients.<sup>[15]</sup> Researchers concluded that a deficiency of vitamin E, zinc and selenium may be risk factors for the development of prostate cancer.<sup>[15]</sup>

#### VITAMIN B<sub>6</sub> (PYRIDOXAL-5'-PHOSPHATE)

Researchers have found that vitamin B6 deficiency results in a significant increase in the uptake of testosterone by the prostate gland.<sup>[16]</sup> This suggests that B6 has a function in the action of testosterone and potentially other steroid hormones, whereby it either reduces the rate of synthesis of testosterone or increases the metabolic clearance.<sup>[16]</sup> This may play an important role in the health of the male prostate gland.

#### RYE (*Secale cereale*) FLOWER POLLEN EXTRACT

A sterol compound called beta-sitosterol is present in the *Secale cereale* pollen extract, and it helps inhibit the aromatase and 5- $\alpha$  reductase synthesis.<sup>[17]</sup> A preclinical study showed the antiproliferative, anticongestive, and anti-inflammatory effects of rye pollen, and these results correlated with the inhibition of the prostaglandin and leukotriene synthesis in the prostate tissues.<sup>[18]</sup>

#### ORGANIC BORAGE (*Borago officinalis*) SEED OIL

Borage seed oil is a crucial source of gamma-linolenic (all *cis*-6,9,12-octadecatrienoic acid [GLA]), an intermediate for important bio compounds such as prostaglandin E, and its derivatives.<sup>[19]</sup> An animal-based study on the Lobund-Wistar rat model of prostate cancer consuming a GLA-enriched diet showed a decrease in tumor growth and prostate growth, estimated by measuring weight, tissue size, DNA content, and prostate-specific antigen.<sup>[20]</sup>

#### L-ALANINE

L-Alanine is one of the nonessential amino acids, and it has a proven therapeutic effect on prostate hypertrophy.<sup>[21]</sup> L-Alanine derivatives, including *N*-stearyl-L-alanine methyl ester (SAM) and *N*-N-stearyl-L-alanine ethyl ester (SAE), proved to be efficient in the palliative treatment of prostate cancer, as it functions as a luteinizing hormone-releasing hormone agonist.<sup>[22]</sup>

#### CRANBERRY (*Vaccinium macrocarpon*) FRUIT

The proanthocyanidins (PACs) present in the cranberry extract led to the attenuation of the expression of PI-3 kinase and AKT proteins.<sup>[23]</sup> In vitro studies on the effect of whole cranberry extract (WCE) on DU145 human prostate cancer cells revealed that it can alter the cell-cycle phase by decreasing the G2-M phase and contrastingly increasing the cell number in that phase.<sup>[24]</sup>

#### L-GLUTAMIC ACID HYDROCHLORIDE

L-Glutamic acid is necessary for purine and pyrimidine synthesis, the key components of DNA and RNA production.<sup>[25]</sup> In a study, four L-glutamic-acid analogues displayed a significant inhibitory effect on prostate cancer PC-3 cell line.<sup>[25]</sup> Similarly, a conjugate molecule of poly-L-glutamic acid (PGA) and an anti-insulin growth factor 1 receptor antibody (AVE1642) showed significant antitumor behavior in prostate-cancer models.<sup>[26]</sup>

#### GLYCINE

Dietary glycine is referred to as a "geroprotector" as its function is to prevent, delay, and reverse aging processes by addressing the underlying cause of aging and age-related diseases to enhance lifespan and health span.<sup>[27]</sup> In a clinical intervention, intake of 3 g of glycine twice a day helped improve the total score for urine storage items on the International Prostate Symptom Score (IPSS) and a significant attenuation of blood pressure and improvement in IPSS quality of life.<sup>[28]</sup>

#### PAU D'ARCO (*Tabebuia heptaphylla*) INNER BARK

Pau d'arco inner bark aids in the activation of the erythroid 2 p45 (NF-E2)-related factor (Nrf2), a transcription factor nuclear factor which plays a critical role of expression of several cytoprotective genes, including NAD(P)H:quinone-oxidoreductase-1 (NQO1) and heme oxygenase 1 (HMOX1).<sup>[29]</sup> An open-label study indicated the safety of 1,050 mg/d of encapsulated pau d'arco was moderate, and it improved the pain intensity scores significantly.<sup>[30]</sup>

#### VITAMIN D<sub>3</sub> (CHOLECALCIFEROL)

A preclinical study on the xenograft prostate cancer mouse model showed that vitamin D<sub>3</sub> had an anticancer effect, which can be explained by its potential to suppress estrogen synthesis and other proinflammatory and growth-signaling pathways.<sup>[31]</sup> A randomized, double-blind clinical study showed that vitamin D<sub>3</sub> supplementation significantly reduced the expression of the proliferation marker Ki67 in prostate cancer.<sup>[32]</sup>

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