

BPH: THE NATURAL APPROACH

There are many conditions for which natural ingredients are therapeutic equivalents to the pharmaceutical alternative. Benign Prostatic Hyperplasia (BPH), in particular, is a condition where natural medicine seems to be far superior to the synthetic drugs, but the answer is more complete than simply Saw Palmetto Extracts.

BPH: A General Review

BPH is an age-related non-malignant enlargement of the prostate gland. It is a hyperplasia, in that it is due to increased numbers of cells, as opposed to a hypertrophy (an increase in cell size). BPH is very common, effecting almost 10% of the men in their 4th decade and increasing every decade thereafter. According to the National Institute on Aging more than half of the men in their 60's have BPH and among men in their 70's and 80's the figure may be as high as 90%.

As the prostate enlarges, it causes compression of the urethra preventing the bladder from adequately releasing urine. Decreased caliber and force of urination are classic signs. Residual urine, distention of the bladder and more frequent urination (especially at night) and urinary tract infections are common. Enlargement of the prostate is usually confirmed by digital rectal examination.

There are two primary features involved with prostate enlargement. The major one being hyperplasia, the non-malignant increase in the number of cells; and the second being prostatitis, the inflammation of the prostate. We shall consider hyperplasia first and then discuss the implications of inflammation.

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Edited By:
Thomas G. Guilliams Ph.D.

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Hyperplasia: Prostate cells, like most cells, are stimulated to grow by various growth factors. Several studies have shown that epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF) are responsible for stimulating prostate cell growth (1,2). Studies have also linked increased levels of bFGF in the prostate with the occurrence of BPH (3). Basically, growth factors are ultimately responsible for the increase in cell proliferation; but they are not the root problem.

While these growth factors are common to many cell types, in the adult prostate they are stimulated primarily through the androgen receptor. The two major androgen hormones involved are testosterone (T) and dihydrotestosterone (DHT). When these hormones bind to the androgen receptors on prostate cells, a complex set of secondary messages are sent that signal the cell to produce and secrete growth factors. These growth factors then bind to growth factor receptors on the same or adjacent prostatic cells, causing another complex set of secondary signals, resulting in mitosis and cell growth (division). Understanding BPH requires an understanding of how all of these factors effect one another, and how the changing hormonal shifts in elderly men relate to BPH.

As men age, serum levels of testosterone drop while the levels of estrogens and prolactin increase. While these may have only subtle effects on other systems, the prostate gland is sensitive to these changes. Both testosterone and DHT bind to the androgen receptor, but DHT binds 5 times stronger than testosterone. Therefore, even though the levels of testosterone are lower, the conversion of testosterone to DHT via the enzyme 5- α -reductase, keeps the androgen receptors activated to stimulate growth factor production. This androgen receptor

stimulation is increased by the action of another hormone, sex hormone binding globulin (SHBG) and estrogen. When SHBG is bound to its receptor on the prostate cells and is also attached to estrogen, it is able to sensitize (or amplify) the androgen signal (4,5,6). In fact, it may be the very minute increase in estrogen levels that convert a normal androgen signal to one that causes hyperplasia. Estrogens also play a role in inhibiting the degradation of testosterone and DHT via hydroxylation. Another factor that may play a role is the increased activity of the 5- α -reductase enzyme, and androgen binding when prolactin is bound to prostatic cells.

Inflammation: Prostatitis describes any inflammation of the prostate, whether it is caused by a bacterial infection or not. Inflammation of the prostate from bacterial infections is often related to BPH since the frequencies of urinary tract infections (UTI) increase as retention of urine in the bladder increases. Both chronic and acute bacterial prostatitis are seen and should be treated much like chronic and acute UTIs. A chronic, non-bacterial prostatitis has also been seen in a large group of men. This form of inflammation seems to be associated with an elevated white blood cell count and abnormal inflammatory cells in the prostate secretion. It is thought that this could possibly be some form of autoimmune response.

Regardless of the type of inflammation, metabolites such as leukotrienes, thromboxanes and prostaglandins; which are derived from arachidonic acid via the lipoyxygenase or cyclooxygenase enzymes are involved. Anti-inflammatory agents that specifically block one or more of these pathways would be helpful in reducing the inflammatory symptoms associated with prostatitis.

TREATMENT:

Several reviews exist on the current treatment approaches to BPH (7,8). What follows is a general overview and not a comprehensive review.

Surgery: Various forms of surgery are available to remove portions of the prostate. These tend to treat the enlargement with good success but have unpleasant side effects such as decreased sexual function (impotence, pain, ejaculatory dysfunction) and bladder incontinence. Newer procedures such as trans-urethral resections or incisions can be done to remove portions of the prostate. These procedures work well for removing portions of the prostate, but do little to address the process that caused the enlargement to begin with. Complications of scar tissue and infections are not uncommon in these procedures.

Drugs: Two types of drugs are primarily used, 5- α reductase inhibitors and alpha andrenoceptor blockers (alpha-blockers). Finasteride (Proscar) is the most used 5- α reductase inhibitor. It blocks the conversion of testosterone to DHT. Finasteride often requires 6 months to a full year before significant results are evident. Alpha-blockers such as terazosin, prazosin and others act by relaxing the muscles around the prostate, relieving many of the symptoms of BPH. While having a more immediate effect on symptoms, it does not change the underlying problems associated with the enlarged prostate (7,8,9)

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Diet: It has been reported that a high protein diet inhibits 5- α -reductase activity, while a low protein diet stimulates the enzyme. No large clinical studies have confirmed these results, and other health conditions may play a greater role in dictating the type of diet for the individual with BPH. It has been shown that the combination of the amino acids glycine, alanine, and glutamic acid relieves many of the symptoms of BPH in several studies. These studies are quite old (10,11), and further research may be warranted as additional support during BPH.

The use of Essential Fatty Acids (EFAs) is important at all times, but BPH sufferers often are deficient in EFAs. The use of EFAs in the form of Flaxseed Oil will provide both omega-3 (linolenic) and omega-6 (linoleic), but much more linolenic. Linolenic acid is a precursor to many of the "good" prostaglandins, which will help suppress much of the prostaglandin-induced inflammation.

Zinc: Zinc intake and absorption is critical for the prostate, especially during BPH. Zinc has been shown to reduce the size of the prostate and the symptoms in many of the patients with BPH (12,13). Zinc is involved in various aspects of androgen metabolism. As has been discussed earlier, estrogen levels are increased in elderly men. Estrogen not only inhibits the hydroxylation of Testosterone and DHT; it also prevents the absorption of zinc. Zinc has been shown to inhibit the activity of 5 α -reductase (14). Zinc also reduces prolactin binding to prostate receptors (15). While the exact levels of supplemental zinc have not been determined experimentally, a dose of approximately 50 mg (325% USRDA) should be both adequate and safe. Since zinc is known to reduce the absorption of copper, it is wise to include copper (1 or 2 mg) with a daily zinc supplementation regimen.

Saw Palmetto Extract: The Liposterolic extract of Saw Palmetto fruits (*Serenoa repens*, or *Sabal serulata*) has been used extensively and for many years as the drug of choice for BPH in Europe and has been getting more and more attention here in the United States. The fatty acids include capric, caprylic, caproic, lauric, palmytic, and oleic. The phytosterols include β -sitosterol, stigmasterol and others. The liposterolic extract of Saw Palmetto has three major activities that improve BPH symptomology, they include: Inhibition of 5- α -reductase (16, 17, 18, 19); Inhibiting the binding of DHT to prostatic cells (20); and Inhibiting both Lipoxigenase and Cyclooxygenase (arachidonic acid cascades) (21). Saw Palmetto, by competing with both the enzyme and receptor that stimulates growth factor secretion, inhibits hyperplasia.

A three-year trial of 309 men, comparing Saw Palmetto Extract to Finasteride (Proscar) showed a significant increase in urinary flow rate and a 50% decrease in residual urine volume associated with the Saw Palmetto group. While the finasteride group also showed improvements, they were not as significant as the Saw Palmetto group, and there were almost 6 times more dropouts in the finasteride group due to unpleasant side effects (22). There have been many clinical trials done with Saw Palmetto extracts showing effective treatment of BPH

Standard dosages of Saw Palmetto Extracts are those which yield from 270 to 305 mg of fatty acids per day (often 320 mg of an 85-95% fatty acid extract). Fatty acid extracts of 85-95% are oil extracts and are in soft gel capsules. Powdered extracts are also available and are usually standardized anywhere from 20% to 55% fatty acids.

Nettles Root Extract: Extracts of Stinging Nettle root (*Urtica dioica* L.) have been used, singly or in combination with other botanicals for the condition of BPH (22, 24, 25). Nettles root extract, as well as Saw Palmetto extract, are both approved by the German government as treatments for BPH. While the mechanism has not been fully elucidated, two activities have been identified in nettle root extracts that may be responsible for the activity. The first is the inhibition of prostate Na⁺/K⁺ ATPase enzyme (26). By inhibiting this crucial enzyme, prostate cells are prevented from proliferating and therefore, this inhibits hyperplasia. The second activity is an interference of the human sex-hormone binding globulin (SHBG). By interfering with SHBG and its receptor, nettles root extracts prevent the estrogen-induced amplification of the androgen signal, which is thought to be one of the major players in BPH (27,28). A common mixture of 120 mg of nettles root extract with 160 mg of saw palmetto is used for many clinical trials.

Pygeum Extract: The Extract of *Pygeum africanum* bark has been used for more than 20 years in France in patients suffering from BPH. The mechanism has not been fully worked out, but a few of the activities are known. Pygeum extracts are known to inhibit the proliferative effects of growth factors such as EGF, bFGF, and IGF-I. This activity was able to inhibit the prostatic growth in an animal model, even when the cells were stimulated to grow (29). This activity makes pygeum extract an excellent synergist with saw palmetto because routes other than the androgen receptor may stimulate growth signals. Additionally, Pygeum extracts antagonize the production of metabolites in the 5-Lipoxygenase pathway (30). This activity will further reduce the inflammatory process in the prostate. Pygeum extracts have been dosed anywhere from 50-200 mg per day with excellent results.

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CONCLUSION:

The natural treatment approach to BPH is one of the triumphs of natural medicine. It is quite unfortunate that more health care professionals have not taken advantage of these approaches with the

millions of patients with this condition. The mechanisms are clear, the results even more clear, and physicians should feel more than confident using any number of products with these ingredients.

IN MY OPINION

As most of you are probably aware, the popularity of St. John's Wort has increased in the past several months. This is directly related to both the Newsweek and 20/20 (ABC) coverage and subsequent local articles. While the increased use of St. John's Wort is welcomed, this event serves to point out just how far behind the American healthcare system is when it comes to botanical medicine. While we have attempted to bring effective phytomedicines into common use by educating doctors, pharmacists, and various regulatory agencies; the public knows nothing of it unless the mass media (or multilevel marketers) covers it. The corresponding frenzy for products results in inferior product being sold by the "get-rich-quick" crowd, improper use and dosing of the standardized products, and a rash of self-diagnosis. Patients are buying and consuming these products in spite of their doctor's concerns, and in some cases against their doctor's "orders." This reveals the key problem. Since most medical doctors have not been sufficiently educated about, or are in many cases opposed to the European style of standardized botanical medicine, patients do not trust their opinion about these matters. By willfully removing this legitimate tool of the health care field from their own hands, they are forcing their patients to get their products and information elsewhere. You can only imagine the ramifications.

*We all know how difficult it is to stay informed, especially with all the misleading information that is currently available. There are many responsible physicians who try to stay informed, but are extremely busy with the tasks of serving their patients. We hope to serve you by publishing **THE STANDARD**, as a concise review of pertinent issues concerning the use of various vitamins, minerals, botanicals, and natural ingredients to promote and maintain the health of your patients.*

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