Prost-P10x®
Ingredient Studies & White Papers

By Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)
Ingredient Studies and White Papers*

Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

Graminex G63®/Cernilton Pollen Extract....3
Quercetin Dihydrate....6
Meriva® Curcumin/Turmeric (Curcuma longa extract)....9
Green Tea Extract (Camellia sinensis 45% EGCG)....14
Beta-sitosterol (plant sterols)....17
Pygeum africanum (bark)....19
Stinging Nettle (Urtica dioica, root)....22
Diindolylmethane (DIM), I3C....25
Vitamin D-3....28
Cranberry (fruit extract)....31
Saw Palmetto Extract (Serenoa repens, (fruit))....34
Zinc....37
References....39
Graminex/Cernilton Pollen Extract and Prostate Health

Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

Pollen extracts (aka cernilton, rye grass pollen, flower pollen, bee pollen) have been shown to have anti-inflammatory properties, a characteristic that makes them helpful in managing benign prostatic hyperplasia (BPH) and prostatitis. Graminex flower pollen extract is a standardized extract of rye pollen (*Secale cereal*), corn pollen (*Zea mays*), and timothy pollen (*Phleum pretense*) and is available around the world under various brand names such as Cernitin ™ (cernilton). (Chambliss 2003) Cernilton has been used to manage prostatitis and BPH in Europe for more than 35 years. It has been shown to be quite effective in several double-blind clinical studies in the management of BPH.

The overall success rate in patients with BPH is about 70 percent. Patients who respond typically have reductions of nocturia and diurnal frequency of around 70 percent, as well as significant reductions in residual urine volume. The extract has been shown to possess some anti-inflammatory activity and cause the bladder to contract while simultaneously relaxing the urethra. In addition, cernilton contains a substance that inhibits the growth of prostate cells.

Numerous scientific studies from North America and Europe have looked at the effects of various pollen extracts on prostate health. Although it is not always easy to distinguish between the different formulas or terms used for the pollen extracts in these studies, the important thing about the studies is that they all involved a pollen extract, and that they demonstrated the ability of this supplement to improve symptoms of BPH and/or prostatitis.

Generally, one major difference between bee pollen and other pollen extracts is that bee pollen is collected by bees from a variety of flowering plants. Along with pollen it also consists of nectar and saliva from the bees, and so the product is not standardized.

Pollen extracts contain pollen from specific plants, which means the end product is standardized; that is, it contains the same amount of active ingredients in each batch. Many of the studies involving pollen and its impact on BPH and/or prostatitis have included the use of cernilton/Graminex, which are explored here, and using a dose of about 500 mg daily.

**Cernilton and Prostatitis**

An early study of cernilton involved 90 men who had chronic prostatitis. The men were divided into two groups: those without complicating factors (72 men) and those with complicating factors (18 men). All the participants took cernilton three times daily for six months and underwent testing (e.g., digital rectal examination, uroflowmetry, bacterial studies) after three and six months of intervention..
Among the men who did not have complicating factors, 56 (78%) reported a favorable response to cernilton: 26 men (36%) had their symptoms eliminated, and 30 (42%) said they had significant improvement, including an increase in urine flow rate. In the group of 18 men who had complicating factors, only one patient reported a response. Overall, cernilton was well tolerated by 97 percent of patients. (Rugendorff 1993)

*European Urology* published a randomized, multicenter, double-blind, placebo controlled phase 3 study compared cernilton (70 patients) with placebo (60 patients) in men who had chronic prostatitis/chronic pelvic pain syndrome. The men received capsules of pollen extract (two capsules every 8 hours) or placebo for 12 weeks.

Compared with placebo, the men who took cernilton reported significant improvements in total symptoms, pain, and quality of life, and they also did not experience any severe side effects. (Wagenlehner 2009) In a subsequent article by some of the same researchers on chronic prostatitis, they reiterated that “preclinical studies on pollen extract have shown effects on smooth muscles of the bladder and urethra, strong anti-inflammatory effects, and antiproliferative effects.” (Wagenlehner 2011)

In *Urology* in January 2006, researchers reported on 60 patients with chronic nonbacterial prostatitis/chronic pelvic pain syndrome patients who were assigned to receive either a pollen extract preparation called Prostat/Poltit (which has ingredients similar to those in cernilton) or a placebo for six months of a double-blind study. After six months, men who received Prostat/Poltit had either no symptoms or significant improvement in symptoms. The authors concluded that the pollen extract was “superior to placebo in providing symptomatic relief in men with chronic nonbacterial prostatitis/chronic pelvic pain syndrome. (Elist 2006)

**Cernilton and BPH**

A double-blind, placebo-controlled study published in the *British Journal of Urology* included 53 men with outflow obstruction due to BPH who took either Cernilton or placebo daily for six months. At the end of the treatment period, 69 percent of the men who took the extract said their symptoms had improved, compared with only 30 percent of the men who took placebo. The improvements included a significant decrease in residual urine and in the antero-posterior diameter of the prostate based on ultrasound.

Flow rate and voided volume did not change significantly between the two groups. The authors concluded that “Cernilton has a beneficial effect in BPH and may have a place in the treatment of patients with mild or moderate symptoms of outflow obstruction.” (Buck 1990)

A total of 89 men with benign prostatic hyperplasia participated in a four-month study in which they received either cernilton (51 patients) or Tadenan (Pygeum, 38 patients). More than three-quarters of men (78%) who received cernilton reported significant improvement in their symptoms compared with 55 percent of the patients who took Pygeum. Patients who took cernilton reported a significant improvement in uroflow rate and a decrease in residual uriner and prostate volume. (Dutkrewicz 1996)
A Japanese study evaluated the use of Cernitin in 79 patients with BPH who ranged in age from 62 to 89 years. Cernitin was administered three times daily, 2 tablets of 63 mg each per dose, for more than 12 weeks. At the end of the study, urine maximum flow rate and average flow rate had increased significantly, while residual urine volume had decreased significantly. Prostatic volume did not change, although 28 men who took Cernitin for longer than 1 year showed a mean decrease of prostatic volume. Improvements in specific factors were as follows: urgency or discomfort 76.9% improvement; dysuria, 71.4%; nocturia, 56.8%; incomplete emptying, 66.2%; prolonged voiding, 64.1%; delayed voiding, 62.2%; intermittency, 60.6%; and postvoid dribbling, 42.7%. Overall, 85 percent of the participants experienced benefit: 11% reported “excellent” results, 39%, “good,” 35%, “satisfactory,” and 15%, “poor.” In conclusion, the authors noted that Cernitin “showed a mild beneficial effect on prostatic volume and urination variables in patients with symptomatic BPH.” (Yasumoto 1995)

The Cochrane Database Systemic Review reported on four studies that involved a total of 444 men who had BPH. The trials lasted from 12 to 24 weeks, and three of the studies used a double-blind approach. All of the studies used cernilton. Overall, cernilton improved urinary symptoms when compared with placebo. Specifically, rye grass reduced the need to get up several times during the night (nocturia) to urinate. The supplement did not, however, improve urinary flow rates or prostate size when compared with placebo. The reviewers concluded from these findings that cernilton “modestly improves overall urologic symptoms including nocturia.” (Wilt 2000)

**How To Use Cernilton/Pollen Extract**

It is recommended that you consult a knowledgeable healthcare provider to determine the best dose of pollen extract for your needs. Anyone who has allergies to grass, flowers, or other plants should talk to their doctor before using pollen extracts.
Quercetin and Prostate Health

Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

Quercetin is a flavonoid whose health benefits include anti-inflammatory and antioxidant properties and the potential to help with prostatitis or chronic pelvic pain syndrome and prostate cancer. This important phytonutrient is found in many plants and foods, most notably red grapes, red wine, apples, tea, berries, and onions. For more than a decade, quercetin has been recognized as a potent antioxidant that has anti-inflammatory and anti-allergy effects by inhibiting the production and release of histamine and other inflammatory factors.

Quercetin is also a possible option to relieve symptoms for men who have prostate problems, and it has been identified as being beneficial in cases of prostatitis in numerous studies, usually at a dose of 500 mg daily.

Chronic Nonbacterial Prostatitis/Chronic Pelvic Pain

In a randomized, double-blind study published in *Urology*, 28 men who had chronic nonbacterial prostatitis/chronic pelvic pain syndrome took either placebo or 500 mg of quercetin twice a day for one month. The authors also conducted a follow-up unblind, open-label study that involved an additional 17 men who received a supplement that contained quercetin, as well as saw palmetto, bromelain, cranberry, and papain ProstaQ).

At the end of the month, the International Prostate Symptom Score (IPSS) fell from 21.0 to 13.1 in the quercetin group and from 20.2 to 18.8 in the placebo group. An improvement in symptoms of at least 25 percent was reported by 20 percent of patient taking placebo and 67 percent of patients taking quercetin. In the 17 patients who took Prosta-Q, 82 percent had at least a 25 percent improvement in their symptom score. Overall, the authors noted that quercetin “provides significant symptomatic improvement” in men who have chronic nonbacterial prostatitis/chronic pelvic pain syndrome. (Shoskes 1999)

Quercetin and Bacterial Prostatitis

A prospective, randomized study was conducted to determine the therapeutic effect of quercetin and curcumin (FlogMEV) and saw palmetto and stinging nettle (ProstaMEV) extracts compared with the antibiotic prulifloxacin in men who had chronic bacterial prostatitis. A total of 143 patients were enrolled, and they were split into two groups: Group A (106 patients) received both prulifloxacin (600 mg daily) plus ProstaMEV and FlogMEV for 14 days; Group B (37 men) received the antibiotic only.

After one month, 89.6 percent of men who received the herbal formulas had no symptoms of prostatitis compared with only 27 percent of the men in the antibiotic-only group. Six months after the intervention portion of the study ended, no patients in Group A had recurrent of
prostatitis compared with two patients in Group B. The authors concluded that the association of quercetin, curcumin, saw palmetto, and stinging nettle extracts can improve the clinical efficacy of prulifloxacin in men who have chronic bacterial prostatitis. (Cai 2009)

**Quercetin and Chronic Prostatitis**

A more recent study was conducted at Cleveland Clinic and included 100 men who had chronic prostatitis/chronic pelvic pain syndrome. The study used a multimodel therapy based on the UPOINT phenotype (e.g., urinary: alpha blocker or antimuscarinic; organ specific: quercetin; tenderness: physical therapy; psychosocial; infection; and neurologic/systemic). The men participated in the therapy for 26 weeks, and the main endpoint was a minimum 6-point decline in NIH-Chronic Prostatitis Symptom Index (CPSI).

A median of 3 UPOINT domains were positive: organ-specific (70%), tenderness (64%), and urinary (59%). At a median 50-week follow-up, 84 percent of the men had at least a 6-point decline in CPSI. The number of domains and initial CPSI were not predictors of a man’s response. Although no one domain predicted outcome, quercetin use was associated with a greater CPSI decrease. (Shoskes 2010) In a subsequent report, Shoskes focused on the advantages of quercetin in treating chronic prostatitis using the UPOINT system, noting that “quercetin can be helpful for those with organ-specific complains (bladder or prostate) and pelvic floor spasm.” (Shoskes 2011)

**Quercetin and Prostate Cancer**

Based on previous research that showed quercetin to possess antitumor activity, investigators at State University of New York at Buffalo studied the effect of quercetin on the ability of prostate cancer cell lines to form colonies. They observed that at concentrations of 25 and 50 micro M, quercetin significantly inhibited the growth of both moderately aggressive DU-145 prostate cancer and highly aggressive PC-3 prostate cancer cell lines, but had no effect on the poorly aggressive LNCaP prostate cancer cell line.

Quercetin also significantly inhibited the expression of certain oncogenes and genes that control specific phases of the cell cycle and “reciprocally up-regulated the expression of several tumor suppressor genes.” The authors concluded that their results “provide a scientific basis for the potential use of flavonoids as nutraceuticals in the chemoprevention of cancer.” (Nair 2004)

Quercetin has also demonstrated the ability to interrupt the spread of prostate cancer (metastases) and to promote cell death. A study published in *Molecular and Cellular Biochemistry* reported that quercetin was able to decrease the activity of specific enzymes known to be involved in tumor invasion and metastases. This finding led the authors to note that quercetin could be developed as a chemopreventive agent for metastatic prostate cancer. (Vijayababu 2006)

The ability of quercetin to promote and enhance cell death in human prostate cancer cell lines has also been shown in several studies conducted at the University of Pittsburgh. (Kim 2007; Lee 2008) A study from the University of Madras suggested that quercetin can decrease the survival of androgen-independent prostate cancer cells by changing the expression of insulin-
like growth factor signaling and inducing apoptosis, which could make the supplement useful in cancer patients. (Senthilkumar 2010)

The University of Kentucky was the setting for another study in which scientists evaluated the effect of quercetin on angiogenesis, which is the formation of new blood vessels that nourish cancer cells. Researchers used quercetin in laboratory tests and mouse models. Overall, researchers found that quercetin inhibited tumor growth and angiogenesis by targeting specific pathways, which indicated that quercetin “could be used as a potential drug candidate for cancer therapy.” (Pratheeshkumar 2012)

**Quercetin and BPH**

In a study published in the *Journal of Endocrinology*, scientists reported on their evaluation of the effect of quercetin and the drug finasteride (Proscar) on the prostate gland in rats. Administration of quercetin (doses of 50, 100, or 150 mg quercetin per kg of body weight) along with finasteride resulted in a 31.8%, 40.0%, and 48.2% reduction, respectively, in prostate weight. The authors concluded that quercetin works with finasteride to reduce prostate weight through a cell cycle-related pathway that may function independent of androgens. (Ma 2004)

**How to Take Quercetin**

Do not exceed 1 gram daily of quercetin without consulting your healthcare provider. Side effects may include headache and stomach upset. (University of Maryland)
**Meriva Curcumin Extract and Prostate Health**

*Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)*

**Director of the Integrative Urological Center, NYU Langone Medical Center**

Curcumin is an active ingredient in the spice turmeric (*Curcuma longa*) and provides prostate health benefits that include help for men who have prostatitis and prostate cancer. The terms “turmeric” and “curcumin” are often used interchangeably, yet they are not the same. Turmeric consists of curcumin as well as other phytochemicals, while curcumin is the main curcuminoid derived from turmeric and is known especially for its potent antioxidant and anti-inflammatory properties. Curcumin is also the substance that gives turmeric its peppery, bitter taste.

Turmeric has a long history of use in both Chinese and Indian medicine practices (for treatment of colds and asthma), and involved turmeric rather than the curcumin derivative alone. More recently, studies have been conducted using both forms and focusing on curcumin and its role in a number of health issues.

**Meriva Curcumin**

Curcumin promises many health benefits, but the challenge lies in getting the curcumin into the body’s cells. Because curcumin has a molecular structure that makes it difficult to be integrated into the bloodstream, it must be modified to achieve optimal absorption or bioavailability. A modified form of curcumin is called Meriva Curcumin Phytosome.

Meriva Curcumin Phytosome is a proprietary form of curcumin that has been formulated to improve absorption. The word “phytosome” refers to plant extracts that are bound to phosphatidylcholine, an important component found in human cells. When you take phosphatidylcholine orally, as in a supplement, it is very well absorbed. Meriva Curcumin Phytosome is a form of curcumin that has been bound to phosphatidylcholine, which makes the phytochemical easily absorbed by the body, where it can quickly reach the cells. Pharmacokinetic comparisons studies of Meriva versus standard turmeric extracts have shown that the phytosome technology improves absorption (bioavailability) up to 20-fold.

In an animal study published in *Cancer Chemotherapy and Pharmacology*, researchers compared Meriva Curcumin with standardized curcumin extract. Rats given Meriva had significantly greater levels of curcumin in their blood and tissue compared with those that received standardized curcumin. In a human study, volunteers were given either 4 grams of a standardized curcumin extract or 450 mg Meriva. Blood levels of curcumin were similar between the two groups despite the wide difference in dosing. (Marczylo 2007)

A December 2012 study compared the use of Meriva curcumin along with standard treatment with standard treatment alone. Sixty-one men with BPH completed the 24-week study: 33 in the Meriva curcumin group and 28 in the control group. Although BPH symptoms improved in both groups, overall results were better in the Meriva group, including quality of life, and there were no significant side effects. (Ledda 2012)
Another advantage of Meriva over standardized curcumin is that it is time-released, which mimics how nutrients are naturally absorbed into the bloodstream after a high-fiber meal. A time-release formula also helps keep blood levels of curcumin more constant and thus requires only twice-a-day rather than more frequent dosing.

Meriva Curcumin also has an important role in maintaining healthy angiogenic balance. Angiogenesis is the formation of new blood vessels in and around cancerous tumors, and the ability of curcumin to maintain angiogenic balance shows it may have a role in fighting cancer.

**Curcumin and Prostatitis**

Curcumin has shown some limited benefit in prostatitis. In a rat study, investigators found that curcumin was effective in managing chronic nonbacterial prostatitis. The researchers believe curcumin was beneficial because it reduced the effect of the pro-inflammatory cytokines interleukin-8 and tumor necrosis factor alpha in the blood and tissues. (Zhang 2010)

A combination of curcumin, quercetin, saw palmetto, and stinging nettle was given to men who had prostatitis in a study published in the *International Journal of Antimicrobial Agents*. Researchers reported that compared with men who received an antibiotic alone, those who took the herbal combination along with the antibiotic had significantly better resolution of their symptoms. (Cai 2009)

**Curcumin and Prostate Cancer**

Scientists at Rutgers, The State University of New Jersey, noticed that in contrast to the high incidence of prostate cancer in the United States, disease incidence in India is very low. It has been suggested that this difference may be related to the fact that Indians consume large amounts of plant-based foods that are rich in phytochemicals, which have been shown to protect against disease.

To test this hypothesis, the researchers used mice that were injected with human prostate cancer cell lines to grow tumors so they could test certain compounds—namely turmeric and phenethyl isothiocyanate (PEITC), a phytonutrient found in cruciferous vegetables (e.g., broccoli, cabbage, kale, cauliflower, turnips, and others). The scientists found that both turmeric (curcumin) and PEITC, in combination and each alone, may be effective in the prevention and treatment of prostate cancer. When the scientists tested the impact of turmeric and PEITC in mice that already had well-established tumors, the phytonutrients alone had little effect, but when they were combined they significantly reduced tumor growth. (Khor 2006)

Inflammation and the spread (metastasis) of prostate cancer were the focus in another laboratory study. Scientists found that curcumin disrupted the inflammation cycle in prostate cancer cells, which resulted in reduced metastasis. (Killian 2012)

An Oregon Health and Science University study published in 2009 reported curcumin has “potential anti-metastatic effects in bone-derived prostate cancer cells.” (Herman) In a Columbia University report, the researchers noted that turmeric “is a novel and potent inducer of apoptosis [cell death] in both androgen-dependent and androgen-independent prostate
cancer cells.” This led the researchers to conclude that “curcumin may provide an alternative, nontoxic modality by which the clinician may prevent the progression of prostate cancer...or to treat advanced prostate cancer by forcing them to undergo apoptosis.” (Dorai 2000)

In a 2010 study in which researchers explored the benefits of several botanicals on prostate cancer, including turmeric, they found that turmeric inhibited growth in both human and animal prostate cancer cell lines. (Slusarz 2010)

More recent research involving curcumin has shown the herb’s potential for slowing tumor growth in men with hormone therapy resistant prostate cancer in a study conducted at Thomas Jefferson University’s Kimmel Cancer Center. In a pre-clinical study, the investigators found that curcumin suppressed two substances known to work against hormone therapy. Specifically, the scientists tested curcumin in two ways. In one test they took prostate cancer cells subjected to hormone deprivation and exposed one sample to curcumin while the other served as a control. They discovered that curcumin boosted the results of hormone therapy while also inhibiting prostate cell survival.

In another experiment, the scientists used a mouse model of prostate cancer resistant to hormone therapy and administered curcumin to one group of mice while the others served as controls. Tumor growth and size were significantly reduced in mice given curcumin. (Shah 2012)

Both curcumin and soy isoflavones were reviewed and reported on in the Korean Journal of Urology. The author noted that curumin and soy isoflavones activate the DNA damage response, which is involved in the development of cancer. This information is important because it provides “an opportunity and rationale for the clinical application of these nutraceuticals in the chemoprevention of prostate cancer.” (Horie 2012)

**Curcumin and Inflammation**

Inflammation has both an upside and a downside. On the upside is something called “normal inflammatory response.” When the body experiences trauma, infection, wear and tear, or other assaults, the immune system steps in and initiates a protective, healing action that involves inflammation. Curcumin’s antioxidant abilities support the body’s normal inflammatory response once it is absorbed into the bloodstream and interacts with various biochemicals in the body.

On the downside, inflammation is typically associated with pain and discomfort as well as other disadvantages. For example, at a symposium regarding the “Pathophysiology of Successful and Unsuccessful Ageing” held in Italy in April 2009, researchers explained that age-related diseases such as cancer, atherosclerosis, metabolic disorders, Alzheimer’s disease, and others are probably caused by low-grade inflammation. Because curcumin has potent antioxidant and anti-inflammatory properties, it could help fight aging in the elderly, as it appears to directly affect major targets, such as reactive oxygen species (ROS, a type of free radical) and certain signaling pathways, which in turn can suppress the pro-inflammatory process involved in aging. (Sikora 2010)
A disease frequently associated with inflammation is arthritis. A review from Oregon Health & Science University, reported there is “limited evidence” indicating that turmeric and curcumin are beneficial for rheumatoid arthritis and other inflammatory conditions. The authors of a March 2012 study, however, reported that when they administered curcumin to patients with rheumatoid arthritis, their findings provided “the first evidence for the safety and superiority of curcumin treatment in patients with active RA.”

In that study, 45 patients were randomly assigned to take 500 mg curcumin, 50 mg diclofenac sodium, or both curcumin and diclofenac. Although the patients in all three groups showed significant improvement in their Disease Activity Score and in American College of Rheumatology factors (i.e., tenderness, joint swelling), patients in the curcumin group had the highest percentage of improvement. (Chandran 2012)

Curcumin has also demonstrated limited effectiveness for people who have familial adenomatous polyposis, inflammatory bowel disease, inflammatory eye diseases, kidney transplantation, and psoriasis. (White 2011)

**Curcumin and Other Benefits**

A study conducted at the University of Texas Medical Branch in Galveston reported on the role of iron and copper neurodegenerative diseases such as Alzheimer’s and Parkinson’s, noting that these metals induce reactive oxygen species (highly active molecules that cause cell damage) while also inhibiting DNA damage repair. One way to fight this “double-edged sword” may be with curcumin. The researchers found that when they exposed iron and copper to curcumin in the lab, the spice bound to the metals and nearly completely reversed the inhibition of DNA repair. (Hegde 2011)

Curcumin may also have a beneficial impact on liver function. The liver plays a critical role in filtering toxins and other harmful substances from the blood. Several studies have indicated that curcumin can protect the liver from environmental toxins through several activities. One way is by increasing the flow and solubility of bile, a fluid that helps with the digestion of fats, as toxins tend to accumulate in fat cells. This benefit also can help in the prevention of gallbladder disease. (Moga 2003) Curcumin also has potent antioxidant power, which not only destroys cell-damaging free radicals but also increases levels of glutathione, a major antioxidant in the liver that is involved in detoxification.

Peptic ulcers may not stand a fighting chance when patients take curcumin. Forty-five patients with symptoms of peptic ulcer (25 of whom had their ulcer identified with endoscopy) were given two 300-mg capsules of turmeric five times daily. At the end of four weeks, 12 of the 25 patients (48%) no longer had evidence of ulcers, and after 12 weeks of treatment, 19 (76%) of the patients were ulcer-free. The remaining 20 patients appeared to have gastritis, heartburn, and erosions. They were treated with turmeric for 4 weeks and reported satisfactory relief during the first two weeks. (Prucksunand 2001)

Aside from its potential role in prostate cancer, curcumin has also demonstrated anticancer activity in other forms of cancer. A 2007 review published in *Advances in Experimental
*Medicine & Biology* reported that “curcumin has been shown to protect against skin, oral, intestinal, and colon carcinogenesis and also to suppress angiogenesis and metastasis in a variety of animal tumor models.” The report also noted that curcumin “inhibits the proliferation of cancer cells by arresting them in the various phases of the cell cycle and by inducing apoptosis.” (Suhr 2007)

Curcumin also may have a role in heart health. Atherosclerosis is a major cause of cardiovascular disease caused by high cholesterol, and doctors typically prescribe statins to lower cholesterol levels. Animal research shows that curcumin can lower plasma cholesterol, low-density lipoprotein cholesterol, and triglyceride levels while also raising high-density lipoprotein levels. Curcumin also suppressed early atherosclerotic lesions.

**How to Use Curcumin**

If you take standardized curcumin powder, the suggested dose is 400 to 600 mg three times daily (University of Maryland). Meriva sustained release (Meriva-SR, 250-mg) can be taken twice daily. Meriva does not contain the flowing agent magnesium stearate, a common additive in supplements, which can inhibit absorption.

Curcumin is considered safe when taken at the recommended doses. However, if you take large amounts for a prolonged time, there is a risk of stomach upset or ulcers. If you have diabetes, consult with your doctor before you take curcumin, because it can lower blood sugar levels.
Green Tea and Prostate Health

Dr. Geo Espinosa, N.D., L.Ac, CCNS, RH (AHG)
Director of the Integrative Urological Center, NYU Langone Medical Center

Green tea (*Camillia sinesis*) is a potent antioxidant and an important tool in the quest for prostate health because of its ability to enhance the immune system, fight prostate cancer, treat prostatitis, and possibly help prevent BPH (enlarged prostate). Green tea’s medicinal powers are attributed to catechins, potent antioxidants that boast an array of health-promoting properties. Catechins have been shown to destroy certain bacteria and viruses, enhance the immune system, and combat several forms of cancer, including prostate cancer. Although there are several different kinds of catechins, the most powerful is epigallocatechin gallate, EGCG. The green tea extract in Prost P10x contains 45 percent EGCG.

**Green Tea, High Grade PIN, and BPH**

It also appears that catechins may benefit men who have pre-cancerous prostate lesions (prostate intraepithelial neoplasia, or PIN), a condition that indicates a high risk of developing “full-on” prostate cancer. Studies indicate that 30 percent of men who have a high-grade PIN go on to develop prostate cancer within one year after repeated biopsy.

In a 2006 study published in *Cancer Research*, 60 men who had high-grade PIN participated in the double-blind, placebo-controlled study. (Bettuzzi 2006) Men in the intervention group received three 200-mg capsules of catechins daily. After one year, only one tumor was diagnosed among the 30 men who took catechins, compared with nine cancers found among the 30 controls. The researchers also noticed that the men who took the catechins had reduced lower urinary tract symptoms, which suggests catechins may be helpful in managing symptoms of BPH.

**Green Tea and Prostate Cancer Benefits**

Studies of large populations of men have shown that those who consume green tea regularly are less likely to develop prostate cancer than men who shun the beverage. (Heilbrun 1986; Jain 1998) In other studies, researchers found that the risk of prostate cancer decreased proportionally as the amount, frequency, and duration of green tea consumption increased. (Jian 2004) In terms of amount of tea consumed, men who drank more than three cups of green tea daily showed a reduced risk of prostate cancer.

In a large study that evaluated the green tea drinking habits of 49,920 men aged 40 to 69 who were followed for at least 10 years, the investigators found that men who consumed five or more cups of green tea daily had a reduced risk of advanced prostate cancer when compared with men who drank less than one cup daily. (Kurahashi 2008)

Research into the impact of green tea on prostate cancer suggests the following:
• It interferes with the activity of an enzyme called ornithine decarboxylase, which plays a role in the “birth” of prostate cancer (Gupta 1999).

• It slows the growth of human prostate cancer cells and prompts them to “commit suicide” (apoptosis) (Gupta 2000).

• It encourages the repair of damaged DNA that might otherwise promote cancer growth (Butt 2009).

• It inhibits the activity of an enzyme called COX-2, which accumulates in prostate cancer tissue and is involved in the prostate cancer process. (Hussein 2005). Research shows that prescription medications called COX-2 inhibitors, such as celecoxib (Celebrex) have the ability to slow the growth of prostate cancer in animal models. However, a recent study published in Clinical Cancer Research shows that the EGCG found in green tea was nearly as effective as COX-2 inhibitors in slowing the growth of prostate cancer. (Adhami 2007).

• It stimulates the activity of certain immune system cells that fight tumors. (Butt 2009).

• A combination of soy protein concentrate and black tea together significantly reduce serum concentrations of both testosterone and DHT in vivo. (Zhou 2003).

• Green tea’s antioxidant properties also contribute to its ability to reduce levels of DHT (dihydrotestosterone), a hormone that raises a man’s risk of developing BPH and prostate cancer.

In a study published in the journal Cancer Prevention Research in June 2009 researchers reported that green tea polyphenols, primarily EGCG, significantly reduced the levels of PSA and two biomarkers for prostate cancer, hepatocyte growth factor (HGF) and vascular endothelial growth factor (VEGF). The study included 26 men who had prostate cancer and who were scheduled for radical prostatectomy. (McLarty 2009).

In the laboratory, green tea components are often the subject of research, as illustrated in a 2012 study published in Carcinogenesis. The scientists set out to determine the reasons why green tea polyphenols have many of the effects mentioned above, such as triggering cell suicide. They reported they had found “new insight into the mechanisms” of green tea polyphenols in human prostate cancer cells and “suggest a novel approach to prevention and/or therapy of prostate cancer” via inhibition of certain enzymes. (Thakur 2012).

**Green Tea and Prostatitis**

The catechins in green tea have also demonstrated an ability to manage prostatitis. In a rat model of chronic bacterial prostatitis, the animals were given either placebo, catechins, ciprofloxacin, or catechins plus ciprofloxacin. The catechins group alone showed modest improvements in inflammation and bacterial growth compared with the placebo group, but the combination of catechins and ciprofloxacin demonstrated significant improvements when compared with placebo. (Lee 2005).
A more recent study of green tea extract and prostatitis was published in the *Journal of Infection and Chemotherapy* in 2010. Researchers used rat models of chronic prostatitis and found that nanocatechins (catechins altered using nanotechnology) had more effective anti-inflammatory and antimicrobial effects on rat chronic prostatitis than “normal” catechins because the body was able to absorb them better. (Yoon 2010)

**How to Use Green Tea**

Green tea’s benefits can be obtained either by drinking the tea or taking supplements, or both. A suggested dose of green tea in supplement form is 500 mg standardized for 45% EGCG. Green tea contains a small amount of caffeine. Anyone who is sensitive to caffeine and who consumes large amounts of green tea may experience some side effects, such as nervousness, insomnia, irritability, and headache.

The amount of catechin in green tea varies depending on where the tea is cultivated, the diversity of plants used, the harvest season, and how it is processed. Generally, Japanese green tea has a greater EGCG content than does Chinese tea, but within these two categories there are differences as well.

According to an analysis of EGCG content in different types of green tea conducted by the authors of *Foods to Fight Cancer*, Sencha uchiyama (a Japanese green tea) is superior to a dozen other Japanese and Chinese green tea varieties. (Beliveau 2007) Other Japanese green teas that rank high in EGCG content include Gyokuro, Sencha, and Matcha. Chinese green tea that is roughly equivalent to Matcha is pito chun emperor; other Chinese green teas that have a lesser amount of EGCG than Matcha and Pilo chun emperor are Hunnan, Yuzan, Paimutan, Meng ding, Lung chin, Dong ding, Pou chong, and Tikuan yin.
Beta-Sitosterol and Prostate Health

Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

Beta-sitosterol is a type of phytosterol (a plant-derived, cholesterol-like substance) with health benefits that include an ability to reduce and treat symptoms of BPH (enlarged prostate), help with urinary and sexual health issues, and possibly assist in fighting prostate cancer. Beta-sitosterol is found in a number of plants, including saw palmetto, rice bran, soybeans, pumpkin seed, peanuts, and pecans. Although beta-sitosterol has a structure similar to cholesterol, it does not act like cholesterol.

Beta-sitosterol appears to act like the prescription drug finasteride (Proscar), which inhibits activity of 5-alpha-reductase and is used to treat BPH. When beta-sitosterol is taken at high doses and along with other sterols, it has been shown to reduce levels of total cholesterol and low-density lipoprotein (LDL) cholesterol by reducing the amount of cholesterol the body absorbs, which in turn may inhibit the production of dihydrotestosterone (DHT). There is also some evidence that beta-sitosterol may boost immunity.

Beta-Sitosterol and BPH

A study from India published in 2012 reported on the effect of beta-sitosterol and scopoletin, both isolated from stinging nettle, on testosterone-induced benign prostatic hyperplasia in rats. After measuring urine output, prostate weight, and other factors over 28 days, the authors concluded that the components of stinging nettle can be an effective drug for the management of BPH. (Nahata 2012)

In a study published in Lancet, 200 men with BPH took 20 mg of beta-sitosterol or placebo three times a day for six months. At the end of six months, the researchers observed an increase in maximum urine flow rate from a baseline of 9.9 mL/second to 15.2 mL/second, as well as a decrease in mean residual urinary volume from 65.8 mL at baseline to 30.4 mL. No changes were reported in men who had taken placebo. (Berges 1995)

After unblinding the 6 month trial from the previous Berges study (1995), men in both the beta-sitosterol and placebo groups were given the option of staying on the trial for an additional 12 months while taking beta-sitosterol. There were 117 men total who were taking 20 mg of beta-sitosterol three times a day. In a follow-up study that evaluated durability of response to beta-sitosterol, the beneficial effects for beta-sitosterol were found to be maintained during an additional 18 months of observation. (Berges 2000)

In 1997, there was a report of a six-month randomized, double-blind, placebo-controlled clinical trial that evaluated the efficacy and safety of 130 mg free beta-sitosterol compared with placebo
in 177 men who had BPH. The International Prostate Symptom Score (IPSS) was the main outcome variable, along with changes in quality of life, peak urinary flow rate (Qmax), and post-void residual urinary volume. After six months, the researchers observed significant improvements over placebo in men who received beta- sitosterol in all factors. The authors concluded that “these results show that beta-sitosterol is an effective option in the treatment of BPH.” (Klippel 1997)

A subsequent review of all existing studies at that time (2000) of beta-sitosterol in men who had BPH was conducted and reported in Cochrane Databases of Systematic Reviews. Four randomized, placebo-controlled, double-blind trials that involved 519 men were evaluated. The investigators found that beta-sitosterols improved urinary symptom scores, peak urine flow, and residual volume. Beta-sitosterols did not reduce the size of the prostate. The reviewers concluded that beta-sitosterols “improve urinary symptoms and flow measures.” (Wilt 1999)

**Beta-Sitosterol and Prostate Cancer**

In the fight against prostate cancer, beta-sitosterol has demonstrated some limited benefit. A study conducted in France showed that beta-sitosterol induced low growth inhibition on prostate cancer cells. (Jourdain 2006)

**How to Use Beta-Sitosterol**

When purchasing beta-sitosterol, make sure the supplement label clearly states the amount of beta-sitosterol in the product. If beta-sitosterol is just one of several plant sterols in the supplement, the beta-sitosterol should make up at least 50 percent of the total amount of sterols in the product. Potential side effects include nausea, gas, and diarrhea.

To increase absorption, beta-sitosterol should be taken on an empty stomach. Typically it takes about two to three weeks before the effects of beta-sitosterol are apparent. The dosage can be reduced once symptoms improve. Consult a knowledgeable healthcare provider for more information on how to use beta-sitosterol.
Pygeum and Prostate Health

Dr. Geo Espinoza, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

Pygeum is an herbal remedy derived from the bark of the Pygeum africanum tree and whose health benefits include an ability to relieve symptoms of BPH (enlarged prostate), as well as possibly helping men who have prostatitis or chronic pelvic pain or prostate cancer. Since ancient times, pygeum has been used to treat bladder problems. Some natives of various South African tribes still use the remedy by boiling the bark of the tree to make a tea. In the 1960s, the Europeans began using a pygeum bark extract to treat mild to moderate BPH. Since then pygeum bark extract has caught the attention of nontraditional healers in other countries.

The major active components of the bark are fat-soluble sterols (phytosterols) and fatty acids. Phytosterols can inhibit the production of DHT (dihydrotestosterone), a hormone that increases the risk of BPH and prostate cancer. Pygeum also reduces the number of receptor sites where DHT can attach to cells.

Virtually all of the research on pygeum has featured a pygeum extract standardized to contain 14% triterpenes including beta-sitosterol and 0.5% n-docosanol. This extract has been extensively studied in both experimental animal studies and clinical trials, and a dose of 100 mg daily has been found to be most effective.

Pygeum and BPH Studies, Pre-2000

An early animal study evaluated the effect of Pygeum africanum in rat prostatic fibroblast proliferation. The investigators found that “therapeutic effect of Pygeum africanum may be due at least in part to the inhibition of growth factors [bFGF, EGF, IGF-I] responsible for the prostatic overgrowth in man.” (Yablonsky 1997)

In an early human study, the efficacy of a Pygeum africanum extract was tested in 263 men who had BPH. The multicenter, double-blind trial was conducted in eight centers in Europe and lasted 60 days. Capsules containing 50 mg of Pygeum africanum extract or placebo were administered twice daily, once in the morning and once in the evening.

At the end of the trial, men who had taken Pygeum extract showed a “marked clinical improvement” in urinary factors (e.g., residual urine, uroflowmetry, nighttime urination), with a 66 percent improvement in urination compared with 31 percent in the placebo group. (Barlet 1990)

Urology published a study in which men with symptomatic BPH participated in a two month randomized, parallel-group, double-blind, comparative phase. Men in group A received 50 mg of pygeum daily while those in group B received 100 mg once daily, followed by a ten-month, open phase, during which men were given 100 mg of pygeum once daily. A total of 209 men...
completed the comparative phase and 174 finished the open phase. Results and safety were similar between groups A and B: both groups had similar improvements in the International Prostate Symptom Score (IPSS; 38% and 35%, respectively), quality of life (28% in both), and maximum urinary flow rate (increase of 16% and 19%, respectively). The authors concluded that “P. africanum extract at 50 mg twice daily and 100 mg once daily proved equally effective and safe at 2 months.” (Chatelain 1999)

A multicenter trial conducted in central Europe explored the efficacy and safety of *Pygeum africanum* extract (available as Tadenan) in men aged 50 to 75 years who had mild to moderate BPH. During the two-month study, the men were administered 50 mg of pygeum extract twice daily. This phase was followed by a one-month period during which none of the men took pygeum.

Eighty-five men completed the entire study. After the two-month phase, IPPS improved 40 percent and quality of life, 31 percent. Nighttime frequency was reduced by 32 percent. These improvements persisted after one month without taking pygeum. No changes were reported in either prostatic volume or quality of sexual life throughout both phases of the study, and no adverse effects related to use of pygeum were noted.

The authors concluded that “under conditions of daily practice, Pygeum africanum extract induces significant improvement in IPSS and uroflowmetry parameters.” (Breza 1998)

**Pygeum and BPH Studies, Post-2000**

Researchers from the Minneapolis Veterans Affairs Center evaluated 18 randomized controlled trials that involved a total of 1,562 men who had BPH. All but one of the trials were double-blinded, and none compared pygeum to standard pharmacologic approaches such as 5-alpha-reductase inhibitors. Overall, the reviewers found that compared with men who took a placebo, pygeum provided a “moderately large improvement” in urinary symptoms and urinary flow measures.

Specifically men who used pygeum were more than twice as likely to report improvement in overall symptoms: residual urine volume improved by 24 percent, peak urine flow increased by 23 percent, and nocturia declined by 19 percent. The conclusion of the researchers was that “a standardized preparation of Pygeum africanum may be a useful treatment option for men with lower urinary symptoms consistent with benign prostatic hyperplasia.” (Wilt 2002)

A review of two studies, conducted at the University of Milan, reported on the results of 70 men who had BPH and who were administered either 320 mg of saw palmetto for 30 days (study 1) or 100 mg *Pygeum africanum* plus 320 mg of saw palmetto for 30 days (study 2). The results of both studies were positive, showing an improvement of about 50 percent in dysuria (painful urination) and frequent urination, and “about a 50% increase in micturition rate with positive effects also in terms of reduction of the micturition rate and of prostate size.” (Mantovani 2010)
In a more recent study, investigators reported on the effects of atraric acid (AA), which they isolated from the bark of pygeum and they found to have an impact on prostate health. The ligand-activated human androgen receptor (AR) plays a key role in supporting the growth of the prostate gland. Thus inhibition of the androgen receptor is a main goal in management of patients.

Investigators at the Institute of Human Genetics and Anthropology found that atraric acid has anti-androgenic activity and inhibits the “transactivation mediated by the ligand-activated human AR.” Specifically, the scientists found that atraric acid can repress the broth of androgen-dependent LNCap and androgen-independent C402 Pca cells, but not prostate cancer cells that lack AR. The authors concluded that their study findings “may serve as a basis for AA derivatives as a new chemical lead structure for novel therapeutic compounds as AR antagonists, that can be used for prophylaxis or treatment of prostatic diseases.” (Papaioannou 2009)

In a subsequent study by many of the same researcher team, the scientists identified the compound N-butylbenzene-sulfonamide (NBBS), isolated from Pygeum africanum, as a specific androgen receptor antagonist. They noted that NBBS has antihormonal activity and the ability to inhibit endogenous PSA expression and the growth of prostate cancer cells. The authors concluded that “NBBS and its derivatives may serve as a novel chemical platform for treatment of prostatitis, BPH and PCa [prostate cancer].” (Papaioannou 2010)

**How to Use Pygeum**

For treatment of BPH, the suggested dosage is 75 to 200 mg capsules of standardized pygeum extract (bark; 13% total sterols) taken daily either as a single dose or divided into two equal doses. Possible side effects of pygeum include nausea, loss of appetite, and abdominal pain. (University of Maryland)
Stinging Nettle and Prostate Health

Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

Stinging nettle (Urtica dioica) is an herb that has anti-inflammatory properties and the potential to be helpful in managing BPH (enlarged prostate), chronic prostatitis, and prostate cancer. The herb has a long history of medical use, especially for urinary tract problems. In addition to its anti-inflammatory properties, stinging nettle is a diuretic, and both of these characteristics make it a good candidate for prostate issues, including urinary tract symptoms associated with BPH.

Laboratory studies have indicated that stinging nettle is comparable to finasteride (Proscar), a drug commonly used to treat BPH, in inhibiting the growth of certain prostate cells. Scientists have not yet determined why stinging nettle root has been shown to reduce symptoms of BPH, although there are several theories. One is that the supplement contains chemicals that have an impact on the hormones testosterone and estrogen, while another suggests the plant’s components work directly on prostate cells.

Stinging Nettle and BPH

In 2012, researchers in India reported on the effect of stinging nettle on testosterone-induced benign prostatic hyperplasia in rats. Over a 28-day period, the investigators measured urine output, prostate weight, and other factors. By the end of the trial, they concluded that stinging nettle can be an effective drug for the management of BPH. (Nahata 2012)

In a six-month, double-blind, placebo-controlled, randomized comparative trial published in the Journal of Herbal Pharmacotherapy, researchers evaluated the effects of stinging nettle and placebo in 558 men who had BPH. The men were evaluated using the International Prostate System Score (IPSS), the maximum urinary flow rate (Qmax), postvoid residual volume, serum prostatic-specific antigen (PSA), testosterone levels, and prostate size. At the end of the six-month trial, 81 percent of men in the stinging nettle group reported an improvement in lower urinary tract symptoms (LUTS) compared with 16 percent of men in the placebo group. In the stinging nettle group, the IPSS declined from 19.8 to 11.8, and in the placebo group it went down from 19.2 to 17.7. Peak flow rates improved by 8.2 mL/second in the stinging nettle group and by 3.4 mL/second in the placebo group. Postvoid residual volume decreased from 73 to 36 mL in men who took stinging nettle, but there was no appreciable change in the placebo group. The size of the prostate also decreased slightly in the men who took stinging nettle but not in those on placebo. At the end of the six month trial, men who had been taking placebo were given stinging nettle, and both groups of men were followed-up at 18 months. Men who continued therapy showed a favorable outcome. (Safarinejad 2005)
In a randomized, double-blind, placebo-controlled multicenter study lasting one year, researchers evaluated the use of Bazoton uno (459 mg dry extract of stinging nettle roots) compared with placebo in 246 men who had BPH. After one year of intervention, the IPSS decreased significantly in the Bazoton uno group compared with placebo. The median Qmax rate increased and the median volume of residual urine decreased in the Bazoton uno group, but neither change was significantly different from those in the placebo group.

The number of adverse events and urinary infections was fewer in the Bazoton uno group compared with the placebo group. The study’s authors concluded that Bazoton uno can be considered a safe option for men who have BPH, especially for reducing irritative symptoms. (Schneider 2004)

**Stinging Nettle and Prostate Cell Growth**

A German study investigated the impact of a 20 percent methanolic extract of stinging nettle roots on the proliferative activity of human prostatic epithelial and stromal (connective tissue) cells using a colorimetric test. The test showed that the stinging nettle extract had a concentration-dependent and significant antiproliferative effect on the epithelial cells during 7 days, but that the stromal cell growth did not change. Inhibition was time-dependent, with the maximum reduction (30%) in growth occurring on day 5 compared to the untreated control. The extract did not demonstrate any cytotoxic effect on cell proliferation. (Konrad 2000)

**Stinging Nettle, BPH, and LUTS**

An October 2010 study from Italy evaluated the use of a botanical combination formula (Pluvio®) containing high amounts of stinging nettle plus avocado and soya oil in men who were surgical candidates to treat lower urinary tract symptoms associated with BPH. One group of men took the natural supplement for six months while the other group took no supplement. After six months, men who had taken the stinging nettle combination had marked improvements in urine flow, quality of life, residual urine, and the need to urinate during the night (nocturia), all without significant side effects. Both PSA and prostate volume were not significantly affected, and no notable side effects were observed. (Bercovich 2010)

**Stinging Nettle, Saw Palmetto, and BPH**

In a recent clinical trial, 257 patients were randomized to receive 160 mg daily of saw palmetto plus 120 mg of stinging nettle (PRO 160/120) twice a day or placebo. The double-blind segment of the study was followed by an open control period of 24 weeks during which all patients were administered the PRO 160/120. Patients randomized to placebo showed a marked improvement in LUTS (as measured by the International Prostate Symptom Score). The tolerability of PRO 160/120 was comparable to the placebo and the authors concluded that PRO 160/120 was clearly superior to the placebo for the amelioration of LUTS. (Lopatkin 2007)

In another study that also used PRO 160/120, a subgroup of 431 patients with early stage BPH was evaluated from a randomized, double-blind, multicenter clinical trial involving 543 patients. The men were randomly given a fixed combination of saw palmetto extract and stinging nettle root (PRO 160/120) or the 5-alpha-reductase inhibitor finasteride (Proscar).
After 24 weeks, the mean maximum urinary flow rate increased by 1.9 mL/second in men who took PRO 160/120 and by 2.4 mL/second in the finasteride group. Men in both groups showed similar improvements in prostate size and in their values on the International Prostate Symptom Score. A safety analysis of 516 patients showed that more men in the finasteride group reported adverse effects than did those in the PRO 160/120 group. The authors concluded that the efficacy of PRO 160/120 and finasteride was similar and unrelated to prostate volume, but that PRO 160/120 had better tolerability than finasteride. (Sokeland 2000)

**Stinging Nettle and Prostatitis**

A prospective, randomized study was conducted to determine the therapeutic effect of saw palmetto and stinging nettle (ProstaMEV) and quercetin and curcumin (FlogMEV) extracts compared with the antibiotic prulifloxacin in men who had chronic bacterial prostatitis. A total of 143 patients were enrolled, and they were split into two groups: Group A (106 patients) received both prulifloxacin (600 mg daily) plus ProstaMEV and FlogMEV for 14 days; Group B (37 men) received the antibiotic only.

After one month, 89.6 percent of men who received the herbal formulas had no symptoms of prostatitis compared with only 27 percent of the men in the antibiotic-only group. Six months after the intervention portion of the study ended, no patients in Group A had recurrent of prostatitis compared with two patients in Group B. The authors concluded that the association of saw palmetto, stinging nettle, quercetin, and curcumin extracts can improve the clinical efficacy of prulifloxacin in men who have chronic bacterial prostatitis. (Cai 2009)

**How To Take Stinging Nettle**

Men who have BPH or suspect prostate problems should not self-treat with stinging nettle but instead consult their healthcare provider. Occasional mild side effects of stinging nettle may include stomach upset, rash, and fluid retention.
DIM and I3C and Prostate Health

Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

DIM (diindolylmethane) and I3C (indole-3-carbinol) are two types of phytonutrients called indoles whose health benefits are related to an ability to reduce symptoms of BPH (enlarged prostate), combat prostate cancer cells, and balance natural testosterone levels in men. Significant amounts of DIM are released in the body when gastric acid acts on I3C during digestion. Indole-3-carbinol is the precursor to DIM and is found in high levels in cruciferous vegetables, such as broccoli, cabbage, and cauliflower. I3C and DIM are frequently taken to promote metabolism of estrogen and to help manage estrogen related conditions, such as cancer. However, DIM has been identified as the safest and most active and effective of the two indoles.

As men age, they experience a decline in testosterone and, in many cases, increases in estrogen levels. The result is a testosterone/estrogen imbalance that directly causes many of the debilitating health problems associated with normal aging. Estrogen is metabolized into several different post-estrogen hormones, namely 2-hydroxy, 4-hydroxy and 16-hydroxy estrogens. Research has shown 4-hydroxy and 16-hydroxy estrogens to be powerful growth and inflammation promoters, with direct connections to cancer, especially in estrogen-sensitive tissues such as the prostate. Obesity is also associated with unfavorable estrogen metabolites. (Schneider 1983) On the other hand, 2-hydroxy estrogens have been shown to be powerfully protective of those same tissues, helping to prevent cancer and resolve disorders including elevated PSA from prostate tissue. (Le 2003)

Balanced estrogen levels in men are essential to encourage a healthy libido, improved brain function, protect the heart and strengthen the bones. However, aging, body fat, hormone replacement, pesticides, prescription medications, and excessive alcohol intake can lead to high estrogen levels, which in turn can cause reduced testosterone levels, fatigue, loss of muscle tone, increased body fat, loss of libido and sexual function, and an enlarged prostate.

DIM acts to promote and support favorable metabolism of estrogen and related hormones by enhancing the liver's ability to metabolize estrogen to "weaker" 2-hydroxyestrone. DIM may reduce prostate cancer incidence by inhibiting the growth of human cancer cells and provoking cell self-destruction (apoptosis). In addition, DIM may improve prostate function, enhance insulin sensitivity, and increase abdominal fat loss.

DIM, I3C and Cancer

A growing body of literature indicates that DIM and I3C have an impact on cancer, including prostate cancer. For example, research shows that I3C has potential value as an anticancer agent for breast cancer through its effect on estrogen receptors. (Wong 1997) Several studies have also shown that I3C can promote cancer cell death (apoptosis), including prostate cancer cells.
A study at Wayne State University examined the molecular mechanisms by which DIM has an effect on prostate cancer cells. The authors noted that they had “previously shown that I3C induces apoptosis and inhibits the activation of NF-kappaB pathway, which could be mediated via Akt signaling pathway.” In the new study, the investigators found that DIM inhibited cell growth and induced apoptosis in PC-3 prostate cancer cells via inhibition of Akt and NF-kappaB activity and their cross-talk. (Li 2005) In a 2006 laboratory study, scientists showed that I3C helped arrest the cell cycle of human prostate cancer cells. (Hsu 2006)

Another research team reviewed laboratory experiments in which they found that I3C and DIM inhibited prostate cancer cell growth and promoted apoptosis. Among their findings was that I3C and DIM upregulated the expression of Phase I and II enzymes, which indicates an increased ability to detoxify and inhibit carcinogens. They also reported that I3C can induce G1 cell-cycle arrest and cell death in prostate cancer cells, and that both I3C and DIM regulate many genes that play a critical role in the control of cell cycle, cell proliferation, signal transduction, and other cellular processes, suggesting I3C and DIM have the ability to impact prostate cancer cells in multiple ways. Based on the results from their laboratory and others, they concluded there is “ample evidence for the benefit of I3C and DIM for the prevention and the treatment of prostate cancer.” (Sarkar 2004)

More recent research continues to see benefits against prostate cancer cells using DIM and I3C. A study from 2012 indicated that both DIM and I3C showed several advantages in prostate cancer cell culture models, including an ability to inhibit cell growth. (Wang 2012) Another study from the same year explained that a formulated DIM called B-DIM had greater bioavailability and along with prompting cell suicide, inhibiting cell growth, and invading prostate cancer cells, could also activate a certain pathway important in prostate cancer. (Chen 2012)

**DIM and BPH**

DIM has also been identified as being potentially beneficial for men who have BPH. In a safety study of both I3C and DIM, supplementation with absorbable DIM resulted in reports of an improvement in prostate function, based on a reduction in nighttime urination, in older men with symptoms of BPH. (Zeligs)

**DIM and Weight**

Research shows that absorbable DIM specifically directs metabolism to produce much higher levels of 2-hydroxy, (Dalessandri 2004) which produces remarkable results in the body, and invigorates the process of weight loss. Lipolysis is the process by which fat cells release stored fat to serve as a primary energy supply. The good estrogen 2-hydroxy helps maintain healthy levels of the catecholamine hormones (epinephrine and norepinephrine) that specifically stimulate enzymes in fat cells to release stored fat for energy. (Ackerman 1981) When given over a period of months in animal studies, 2-hydroxy estrogen prevented obesity and the Metabolic Syndrome. (Tofovic 2001)
Research with absorbable DIM has shown that supplementation before exercise results in greater lipolysis in the hours following exercise and enhances weight loss in adults on a weight loss program. (Zeligs 2003)

Both indole-3-carbinol and DIM are available in supplement form, although absorbable DIM is generally recommended as the more direct and effective form, as only about 10 percent of I3C supplement is converted to DIM in the gut. Use of indole-3-carbinol is also associated with side effects, such as dizziness and unsteady gait, while DIM is not.
Vitamin D and Prostate Health

Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

Vitamin D has many important health benefits regarding prostate health, including assistance in relieving symptoms of BPH (enlarged prostate), prostatitis or chronic pelvic pain syndrome, and prostate cancer. The nutrient also performs many critical roles in the body, such as help in building strong bones by assisting in the absorption and use of calcium and phosphorus, and maintaining proper nerve function.

Most people have low levels or are deficient in vitamin D, mainly because they do not get sufficient sunlight (the best source of vitamin D) and/or they do not eat enough foods that contain the vitamin. Food, however, is not the best way to meet the body’s requirement for this vitamin, which is why sunlight and supplements are important. The US government’s recommendation for vitamin D is 200 IU daily. Many experts, however, believe this figure is too low, including the Vitamin D Council, which recommends 5000IU a day.

Vitamin D3 is indirectly derived from lanolin (a fat found in sheep wool). When the sheep are sheared, the wool is washed and lanolin is gathered. A molecule from lanolin can then be synthesized into vitamin D3. There is no lanolin in the end product. Vitamin D3 is not found in large quantities in milk; milk happens to be a good source of vitamin D3 only because milk manufacturers add it.

Vitamin D and Prostate Cancer

The relationship between vitamin D and prostate cancer is controversial. For example, results of the largest and most comprehensive study to date (February 2011) were reported by scientists at the University of Bristol. After reviewing more than 24,000 papers and evaluating the data regarding vitamin D and prostate cancer in 25 papers, they concluded “Published literature provides little evidence to support a major role of vitamin D in preventing prostate cancer or its progression.” (Gilbert 2011)

Numerous previous studies do not agree, however. One of those studies was published in November 2009 in BJU International, in which 26 men who had current prostate cancer were given a daily dose of vitamin D. The PSA levels in five men declined: two by more than 50 percent, two by 25 to 50 percent, and one by less than 25 percent. In the remaining patients, their PSA levels stabilized after treatment with vitamin D for up to 36 months. The investigators did not observe a significant correlation between response to vitamin D and stage of disease, Gleason grade, previous treatments or PSA level at diagnosis or initiation of vitamin D supplementation. However, the authors concluded that “Vitamin D therapy is an effective and well tolerated treatment for patients with asymptomatic progressive prostate cancer, and is a useful addition to the therapeutic options.” (Newsom-Davis 2009)
Stanford University School of Medicine was the site for a review that highlighted the anti-inflammatory capabilities of calcitriol, the hormonally active form of vitamin D. The authors pointed out that calcitriol inhibits both the synthesis and the proinflammatory actions of prostaglandins and suppresses the production of proinflammatory cytokines in prostate cancer cell studies. Calcitriol can also inhibit tumor angiogenesis, invasion, and metastasis (spread). Based on these findings, the authors hypothesized that the anti-inflammatory actions of calcitriol, “in addition to the other known anti-cancer effects of calcitriol, play an important role in its potential use as a therapeutic agent for PCa [prostate cancer],” and that it “should be evaluated in clinical trials in PCa patients with early or precancerous disease.” (Krishnan 2010)

A 2013 report noted an association between vitamin D and the risk of prostate cancer. The National Cancer Institute study noted that the main vitamin D carrier protein, called vitamin D-binding protein (DBP), has an impact on prostate cancer. That is, high levels of DBP was associated with a significantly decreased risk of prostate cancer in men with lower concentrations of vitamin D (25(OH)D) and an increased risk in men with higher vitamin D concentrations. (Weinstein 2012)

**Vitamin D and BPH**

The relationship between vitamin D and BPH has been evaluated in a number of trials. One study evaluated 4,770 participants in the Prostate Cancer Prevention Trial who were free of BPH at baseline. Over seven years, 876 incident BPH cases were documented. When the investigators analyzed factors such as diet, alcohol, and supplement use via a food frequency questionnaire, they determined there were no associations between supplemental antioxidants and BPH risk, and there was “weak evidence for associations of lycopene, zinc, and supplemental vitamin D with reduced risk.” (Kristal 2008)

At least one study has reported that a low level of vitamin D circulating in the blood is linked to a greater risk of having an enlarged prostate or prostate cancer. An epidemiological study of 977 randomly chosen men investigated the prevalence of prostate disease based on blood samples, a questionnaire, and physical examination. Investigators found a 23.1 percent prevalence of BPH, 5.1 percent of prostatitis, and 3.7 percent of prostate cancer. Among other discoveries, the authors reported finding lower levels of vitamin D in men who had BPH and prostate cancer. Because vitamin D inhibits cellular proliferation, the authors noted that “lower levels are confirmatory with its loss of protective role against prostate cancer.” (Galic 2008)

Additional evidence can be found in a study conducted in Italy in which researchers identified how the vitamin D receptor agonist elocalcitol, a synthetic derivative of vitamin D3, is capable of stopping growth of the prostate in men who have BPH. The process by which elocalcitol both stops inflammation and the growth of BPH cells is complex, and involves elocalcitol’s ability to significantly inhibit production of IL-8, a substance involved in BPH pathogenesis, by BPH cells stimulated with inflammatory cytokines, and IL-8-induced proliferation of BPH cells. The authors concluded that their data “provide a mechanistic explanation for the anti-proliferative and anti-inflammatory properties of elocalcitol in BPH cells.” (Penna 2009)

**Vitamin D and Prostatitis**
A review published in the *International Journal of Andrology* noted that scientists are beginning to appreciate chronic inflammation as a potentially important factor in men who have BPH, as well as the role of bacterial and nonbacterial chronic prostatitis. The authors also pointed out that “the mechanism of action of VDR [vitamin D receptor] agonists supports an important role of chronic inflammation in BPH pathogenesis and strengthens the concept of these agents as a therapeutic option for pharmacological treatment of BPH.” (Fibbi 2010)

The *Journal of Autoimmunity* recently published a study on prostatitis and vitamin D, in which investigators explored the effect of vitamin D receptor silencing on the development of experimental autoimmune prostatitis in mice. They concluded that “vitamin D receptor modulation holds the promise of interfering with autoimmune prostatitis.” (Motrich 2009)

**How To Take Vitamin D**

The Vitamin D Council recommends that people take 5,000 IU daily for 2 to 3 months, then ask their healthcare provider for a 25-hydroxyvitamin D test to check their levels. Once individuals know their body’s level of vitamin D, they can adjust the dosage until their blood levels are between 50 and 80 ng/mL. That is the healthy range recommended by the Vitamin D Council and some other experts.
Cranberry and Prostate Health

Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

Cranberries (*Vaccinium macrocarpon*, the American cranberry) offer significant health benefits, including help in preventing urinary tract infections and in the treatment of prostate health issues such as BPH (enlarged prostate), prostatitis, or chronic pelvic pain syndrome. These tart fruits have been valued for their healing abilities for centuries and were favored by the Native Americans, who used them to treat bladder and kidney conditions. Cranberries are related to blueberries, buckberries, and huckleberries and are an excellent source of antioxidants, including substances called proanthocyanidins (PACs), as well as vitamin C.

Cranberries are not the only food that contains PACs; apples, chocolate, green tea, grapes, and maritime pine bark (Pycnogenol) are also good sources of the phytonutrient. However, the main type of PACs in cranberries is called A-type PACs, which differs from those found in other foods, which are called B-type PACs. These B-type PACs are what make cranberries special regarding prostate health and especially urinary tract health.

**Cranberry and Urinary Tract Health**

Only the PACs in cranberries have the ability to prevent bacteria from adhering to the walls of the urinary tract, which is the essential characteristic that makes cranberries so helpful in managing urinary tract infections. French scientists measured the PACs in cranberries using a method called the 4-dimethylaminocinnamaldehyde (DMAC). Then in 2004, France became the first country to approve a health claim for the American cranberry, noting that use of at least 36 mg of proanthocyanidins can “help reduce the adhesion of certain *E. coli* bacteria to the urinary tract walls.”

Numerous studies since then have demonstrated the ability of cranberries to help manage urinary tract infections, supporting the use of cranberry supplements or juice (unsweetened) for this purpose. A study (March 2011) published in *Current Bioactive Compounds* reported on the success of a whole cranberry powder product (PACran from Decas Botanical Synergies) that significantly reduced the recurrence of urinary tract infections when administered in two different doses.

The 90-day randomized clinical trial involved 60 women aged 18 to 40 years who had a history of recurrent urinary tract infection, the presence of *E. coli*, and mild symptoms of urinary tract infection. The women were randomly assigned to receive no treatment, 500 mg of whole cranberry powder daily, or 1,000 mg of whole cranberry powder daily.

After 10 days and at the end of 90 days, all the women underwent a urine culture analysis. The women who did not receive any treatment showed no changes in the concentrations of *E. coli*, while those in the two cranberry treatment groups showed reductions of *E. coli* of between 25
and 45 percent after 10 days of taking whole cranberry powder. This reduction persisted over 90 days.

Forty percent of the women in the two cranberry treatment groups also reported complete relief and remission from urinary tract symptoms such as frequent urination, as well as from itching and burning during urination. Based on all of these findings, the study’s authors concluded that “proanthocyanidins standardized whole cranberry powder was effective in safely reducing the number of \textit{E. coli} positive subjects at both the 500 mg and 1000 mg dose levels and in ameliorating the symptoms of UTI in these subjects. Therefore, a daily dose of 500 mg or 1000 mg of proanthocyanidins standardized whole cranberry powder may be considered as an adjunct to antibiotic prophylactic therapy against recurrent UTIs.” (Sengupta 2011)

The 500-mg dose used in this study reportedly provides the same amount of anti-adhesion activity against \textit{E. coli} over 24 hours as does 300 milliliters of Cranberry Juice Cocktail that contains 36 mg proanthocyanidins, based on the earlier French health claim.

Another study was published in the journal \textit{BMC Infectious Diseases}. (Howell 2010) The researchers noted that cranberry powder standardized to deliver 72 mg proanthocyanidins per day was effective in preventing adhesion. Several earlier studies by Howell at the Marucci Center for Blueberry and Cranberry Research and Extension, Rutgers, The State University of New Jersey, isolated and studied the effects of A-type PACs from cranberry and their antiadhesion activity against \textit{E. coli}. (Howell 2007; Howell 2002) The ability of cranberry to treat urinary tract infections, however, has not been proven.

**Cranberry and Prostate Health**

Several other studies indicate that cranberry may be helpful in managing prostatitis and BPH. One was conducted in the Czech Republic and included 42 men at risk of prostate disease because they had lower urinary tract symptoms (LUTS), elevated prostate specific antigen (PSA), negative prostate biopsy, and chronic nonbacterial prostatitis. The participants were given either 1,500 mg of dried powdered cranberries per day for six months or no cranberry supplement. Compared with the control group, men who had taken the cranberry supplement had statistically significant improvement in International Prostate Symptom Score (IPSS), quality of life, urination factors (e.g., rate of urine flow, average flow, total volume, post-void residual urine volume), and lower total PSA levels at the end of the six-month study.

Cranberry had no effect on blood testosterone or serum C-reactive protein levels. Men in the control group showed no statistically significant improvement. The authors noted that their results were “the first firm evidence that cranberries may ameliorate LUTS, independent of benign prostatic hyperplasia or C-reactive protein level.” (Vidlar 2010)

In another study, 48 rats with chronic bacterial prostatitis (CBP) were administered \textit{E. coli} extract, cranberry, ciprofloxacin, or no intervention. After four weeks, the scientists analyzed the results of microbiological culture of prostate and urine samples along with histological findings for the prostate for each group of rats. They found that the infection rate in the ciprofloxacin group was significantly lower than the rate in the control group, and that the \textit{E. coli} and cranberry groups showed significantly reduced bacterial growth and prostatic inflammation.
when compared with the control group. Based on these observations, the authors concluded that “E. coli extract has a potential preventive effect on the development of CBP, and cranberry also exhibits promising activity in this context.” (Kim 2010)

Among men undergoing radiation therapy for prostate cancer, LUTS can be a significant problem. Daily use of cranberry extract supplements during 6 to 7 weeks of radiation therapy was found to be highly effective in reducing the incidence of LUTS in one study. Only 8.7% of 184 men who took cranberry extract experienced LUTS compared with 24.2% of 186 controls. (Bonetta 2012)

Use of cranberry in the fight against prostate cancer is in its preliminary stages and limited to lab and animal studies, but the research is worth noting. In one study, Canadian researchers found that whole cranberry extract was effective in causing cell suicide (apoptosis) in human prostate cancer cells. (MacLean 2011) Another Canadian study found that whole cranberry extracts effectively reduced cell cycle activity of human prostate cancer cells. (Deziel 2012)

**How to Use Cranberry**

The dose of cranberry found to be most beneficial in supporting urinary tract health and managing urinary tract symptoms is 500 mg daily. Cranberry is considered safe with no serious side effects. However, because cranberry contains high levels of oxalate, chemicals that can increase the risk of kidney stones, consult your doctor before taking cranberry if you have had kidney stones. Cranberry may also interfere with the effects of blood-thinning drugs.
Saw Palmetto and Prostate Health

Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

Saw palmetto (Serenoa repens/Sabal serrulata, also known as the American dwarf palm tree) offers health benefits that include help with symptoms of BPH (enlarged prostate), as well as relief of urinary tract symptoms and some ability to help with prostate cancer. This herbal remedy has been valued for centuries for treatment of prostate and urinary problems. Today, saw palmetto is still widely used for the same purposes throughout Europe and the United States, but most especially for BPH, for which a daily dose of 320 mg has been found to be most effective.

Among the main compounds of saw palmetto are fatty acids and sterols, the latter of which include beta-sitosterol, a substance found to be effective in the treatment of BPH and an ingredient also found in the supplement Prost P10x. Beta-sitosterol works by inhibiting the activity of 5-alpha-reductase. Saw palmetto also reduces levels of DHT (dihydrotestosterone), which is associated with BPH, by blocking the activity of 5-alpha-reductase and receptor sites on cell membranes that the cells need to absorb DHT. The ability of saw palmetto to improve symptoms of BPH, as well as act against prostate cancer cells, has been illustrated in a number of published studies.

Saw Palmetto and BPH Symptoms

Investigators at the University College London published (2013) the results of a study in which they evaluated the impact of saw palmetto on BPH symptoms and sexual dysfunction. Eighty-two men participated in the eight-week trial, and each took 320 mg saw palmetto extract daily. By the end of the study, their International Prostate Symptom Score (IPSS) had declined significantly and their sexual dysfunction and quality of life scores also improved. The authors claimed “this was the first trial with saw palmetto to show improvement in BPH symptoms and SDys [sexual dysfunction] as well.” (Suter 2013)

A 2011 study evaluated the long-term efficacy of treatment with a saw palmetto extract (Prostamol Uno) in men who had lower urinary tract symptoms (LUTS) associated with BPH. A total of 120 patients with mild or moderate LUTS were treated daily for 24 months with one capsule of 320 mg ethanolic extract of saw palmetto. At the end of the treatment period, the men showed a statistically significant improvement in their International Prostate Symptom Scores (5.5 points), quality of life, Qmax, International Index of Erectile Function (IIEF; 6.4 points), and reduction in residual urinary volume. Prostate volume had declined from a mean of 39.8 mL at baseline to 36 mL at 24 months. The study’s authors concluded that long-term treatment with 320 mg of ethanolic saw palmetto extract is effective in reducing urinary obstruction,
improving LUTS and quality of life, and also has a positive impact on sexual function, illustrated by the statistically significant increase in the IIEF. (Sinescu 2011)

**Saw Palmetto and Tamsulosin**

A double-blind trial published in European Urology in 2002 indicated that saw palmetto is effective in reducing BPH symptoms. A total of 704 men who had BPH were randomly assigned to receive either saw palmetto berry extract (320 mg daily) or the medication Flomax (tamsulosin, 0.4 mg daily). All the men were treated for one year, and throughout the year their I-PSS (International Prostate Symptom Score), Qmax (peak urinary flow rate), and quality of life were evaluated periodically. At the end of 12 months, the results showed that saw palmetto and tamsulosin produced similar improvements in symptoms, although prostate volume decreased slightly in the saw palmetto treated men. Both saw palmetto and tamsulosin were well tolerated, but ejaculation disorders occurred more often in the tamsulosin group. (Debruyne 2002)

**Saw Palmetto and Finasteride**

In a study recently published in Advances in Therapy, researchers reported that a saw palmetto extract (SPET-085) effectively inhibited 5-alpha-reductase and that its effect was similar to that of a prescription drug, finasteride, that is used for this purpose in BPH. The study was conducted in a lab and involved the use of a saw palmetto extract in a cell-free test system, in which scientists measured the inhibitory potency of the extract against 5-alpha-reductase isoenzyme type II and compared it with that of finasteride. Results showed that the saw palmetto extract effectively inhibited the enzyme and that the amount of extract required was very low compared to data associated with other saw palmetto extracts tested in others studies. The researchers also reported that the prostate health-promoting activity of SPET-085 corresponded to that of the standard drug therapy, finasteride. (Pais 2010)

**Saw Palmetto and BPH Surgery**

Saw palmetto also appears to benefit men who are scheduled to undergo surgery for BPH. A study from the University of Milan showed that men who took saw palmetto for two months prior to transurethral resection of the prostate or prostatectomy experienced significantly reduced intra- and postoperative complications compared with men who did not take the supplement.

The 120 men in the study were randomly assigned to take either 320 mg of saw palmetto (Permixon) daily for two months before their surgery or to undergo surgery without taking the supplement. After the surgeries were performed, the authors noted no intraoperative complications in the treatment group versus 15 percent in the control group. The need for transfusion was also remarkably lower in the treatment group (0%) compared with controls (38.33%). Men in the saw palmetto treatment group also required significantly shorter duration of catheterization (64.95 hours vs 91.7 hours in controls) and a significantly shorter length of hospitalization (5.92 days) compared with controls (7.92 days). The authors conclude that saw
palmetto prior to surgery for BPH effectively reduces intraoperative and postoperative complications. (Anceschi 2010)

**Saw Palmetto and Pygeum**

The University of Milan was the site of a review of two studies that evaluated a total of 70 men who had BPH and who were treated with either saw palmetto or pygeum. In one study, the men were treated with 320 mg per day of saw palmetto for 30 days; in the other study, patients received either 320 mg per day of saw palmetto or four 25-mg capsules of Pygeum africanum (Tadenan) per day for 30 days. The men in both studies experienced about a 50 percent improvement in dysuria (painful urination) and in frequent urination. They also reported about a 50 percent increase in urination rate with positive effects, a reduction in prostate size, and good tolerability of the supplements. (Mantovani 2010)

**Saw Palmetto and Prostate Cancer**

Two recent Italian studies have reported on the impact of saw palmetto extract on prostate cancer cells. In one, investigators compared the effects of saw palmetto extract in two human prostate cancer lines (PC3 and LNCaP) as well as a breast cancer cell line, with emphasis on the role of the mitochondrial apoptotic (cell death) pathway. The investigators found that the prostate cancer cells treated with saw palmetto extract, but not the breast cancer cells, underwent cell death.

Within minutes of adding saw palmetto extract to the prostate cells, the permeability transition pore opened, which led to the cells’ eventual death by 24 hours later. (Baron 2009) In the second study, scientists evaluated the effects of saw palmetto extract (Permixon) on proliferation and apoptosis of androgen-independent prostate cancer cells. One hour after administering the saw palmetto extract, the investigators observed a marked reduction in the mitochondrial potential, a decline in cholesterol, and modification of the phospholipid composition, including a significant decrease in omega-6 content. They noted that the decrease in omega-6 content could be responsible for the prolonged and consistent increase in the apoptosis rate and the inhibition of proliferation present after 2 to 3 days of treatment with saw palmetto extract. (Petrangeli 2009)

**How To Use Saw Palmetto**

A suggested dose for saw palmetto is 320 mg daily of extract standardized to contain 85 to 95 percent sterols and fatty acids. (University of Maryland) Men who use saw palmetto may experience some back pain, headache, and erectile difficulties.
Zinc and Prostate Health

Dr. Geo Espinosa, N.D., L.Ac, CNS, RH (AHG)

Director of the Integrative Urological Center, NYU Langone Medical Center

Zinc is a mineral whose health benefits associated with prostate health include sexual development and reproduction, as well as a role in BPH (enlarged prostate), prostatitis or chronic pelvic pain syndrome, and prostate cancer. In addition, zinc helps keep the immune system strong, memory intact, cholesterol and blood sugar in line, and blood pressure and heart beat regulated.

It is believed that a deficiency of zinc may result in an increase in infections and prostatitis, or it may make a male susceptible to prostate cancer because the mineral is also a key player in the body’s DNA-damage repair process. Thus the role of zinc in prostate cancer has been an area of research.

Zinc and Prostate Cancer

In the Chinese Journal of Cancer Research, scientists reported on the impact of zinc citrate on hormone resistant prostate cancer. The study was conducted using human prostate cancer cell lines. Treatment of the cells with a zinc citrate compound prompted cell death by having an effect on certain proteins. (Hong 2012)

In a University of Washington Cancer Prevention Program study, researchers analyzed the relationship between dietary and supplemental zinc and prostate cancer using the VITamins And Lifestyle (VITAL) cohort. Of 35,242 men who completed the dietary and supplemental questionnaire, 832 men developed invasive prostate cancer over a four year period. The investigators did not observe a reduced risk of prostate cancer associated with a ten-year average intake of supplemental zinc greater than 15 mg per day, but they did see a decreased risk of advanced prostate cancer with a greater intake of supplemental zinc (greater than 15 mg daily vs no zinc supplement). No association between dietary zinc and prostate cancer risk was seen. (Gonzalez 2009)

A study conducted in Venezuela set out to determine zinc concentrations in the prostatic fluid of men who had prostate problems (30 subjects) compared with healthy controls (10). The researchers found that zinc concentrations in men who had prostatitis and prostate cancer—but not BPH—were lower than those in the controls. This finding led them to “consider the possibility of recommending zinc supplements as a coadjuvant therapy in patients with prostatitis,” and to use zinc levels as a diagnostic tool to distinguish BPH from prostate cancer. (Gomez 2007)
**Zinc and Laboratory Studies**

Researchers at the University of Maryland (Baltimore) showed that exposing human prostate cancer and BPH cells to zinc induced cell suicide, and they identified the specific genes involved. Thus this study provided an extensive database on zinc-related prostate cancer research, and the results suggested zinc regulation of gene expression is cell-type specific; that is, the genes Fos, Akt1, Jak3, and PI3K showed themselves to be highly regulated by zinc. (Lin 2009)

In a similar vein, Oregon State University was the setting for a study that evaluated the antiproliferative effects of zinc in both prostate cancer cells and benign prostatic hyperplasia cells. Based on the knowledge that zinc concentrations in the prostate are “uniquely high” but significantly low in the presence of prostate cancer, the study’s authors set out to evaluate the antiproliferative effects of zinc in prostate cancer cells and BPH cells, with the goal of identifying possible mechanisms.

Both prostate cancer and BPH cells were treated with zinc for 24 and 48 hours, and cell viability and growth were observed. BPH cells were more sensitive than were prostate cancer cells to zinc’s antiproliferative effects. The authors concluded that the differential response to zinc in the prostate cancer and BPH cells “suggests that zinc may serve an important role in regulating cell growth and apoptosis in prostate cancer and hyperplasia cells.” (Yan 2010)

**How To Use Zinc**

Although zinc sulfate is the most frequently used zinc supplement (and also the most inexpensive), it is not easily absorbed. Therefore the preferred form is zinc citrate, which is more bioavailable. The daily requirement for zinc is 11 mg for adult males.

Foods that contain a good level of zinc include oysters (extremely high levels), beef, poultry, seafood, fortified cereals, calf’s liver, sesame seeds, pumpkin seeds, crimini mushrooms, and low-fat yogurt. Zinc is typically found in multimineral supplements, but is also available alone.
References

Graminex G63®/Cernilton Pollen Extract


Drug.com website: http://www.drugs.com/npc/bee-pollen.html


Quercetin dehydrate

Cai T et al. Serenoa repens associated with Urtica dioica (ProstaMEV) and curcumin and quercetin (FlogMEV) extracts are able to improve the efficacy of prulifloxacin in bacterial prostatitis patients: results from a prospective randomized study. Int J Antimicrob Agents 2009 Jun; 33(6): 549-53

Kim YH, Lee YJ. TRAIL apoptosis is enhanced by quercetin through Akt dephosphorylation. J Cell Biochem 2007 Mar 1; 100(4): 998-1009


Nair HK et al. Inhibition of prostate cancer cell colony formation by the flavonoid quercetin correlates with modulation of specific regulatory genes. Clin Diag Lab Immunol 2004 Jan; 11(1): 63-69

Senthilkumar K et al. Quercetin regulates insulin like growth factor signaling and induces intrinsic and extrinsic pathway mediated apoptosis in androgen independent prostate cancer cells (PC-3). Mol Cell Biochem 2010 Nov; 344(1-2): 173-84


University of Maryland Medical Center: http://www.umm.edu/altmed/articles/quercetin-000322.htm


**Meriva® Curcumin/Turmeric (Curcuma longa extract)**

Cai T et al. Serenoa repens associated with Urtica dioica (ProstaMEV) and curcumin and quercetin (FlogMEV) extracts are able to improve the efficacy of prulifloxacin in bacterial prostatitis patients: results from a prospective randomized study. Int J Antimicrob Agents 2009 Jun; 33(6): 549-53


Marczylo T et al. Comparison of systemic availability of curcumin with that of curcumin formulated with phosphatidylcholine. Chemother Pharmacol 2007, 60, 171-177


Sikora E et al. Curcumin, inflammation, ageing and age-related diseases. *Immun Ageing* 2010 Jan 17; 7(1): 1


University of Maryland: [http://www.umm.edu/altmed/articles/turmeric-000277.htm](http://www.umm.edu/altmed/articles/turmeric-000277.htm)


Zhang QY et al. Reducing effect of curcumin on expressions of TNF-alpha, IL-6 and IL-8 in rats with chronic nonbacterial prostatitis. *Zhonghua Nan Ke Xue* 2010 Jan; 16(1): 84-88

**Green Tea Extract (Camellia sinensis 45% ECGC)**


Thakur VS et al. Green tea polyphenols causes cell cycle arrest and apoptosis in prostate cancer cells by suppressing class I histone deacetylases. *Carcinogenesis* 2012 Feb; 33(2): 377-84

University of Maryland Medical Center: [http://www.umm.edu/altmed/articles/green-tea-000255.htm](http://www.umm.edu/altmed/articles/green-tea-000255.htm)

**Beta-sitosterol (plant sterols)**


Nahata A, Dixit VK. Ameliorative effects of stinging nettle (Urtica dioica) on testosterone-induced prostatic hyperplasia in rats. *Andrologia* 2012 May; 44 Suppl 1:396-409


**Pygeum africanum (bark)**


Papaioannou M et al. NBBS isolated from Pygeum africanum bark exhibits androgen antagonistic activity, inhibits AR nuclear translocation and prostate cancer cell growth. *Invest New Drugs* 2010 Dec; 28(6): 729-43


University of Maryland Medical Center: [http://www.umm.edu/altmed/articles/benignprostatic-000018.htm](http://www.umm.edu/altmed/articles/benignprostatic-000018.htm)


**Stinging Nettle (Urtica dioica, root)**

Bercovich E, Saccomanni M. Analysis of the results obtained with a new phototherapeutic association for benign prostatic hyperplasia versus controls. *Urologia* 2010 Oct 2; 77(3): 180-86

Cai T et al. Serenoa repens associated with Urtica dioica (ProstaMEV) and curcumin and quercitin (FlogMEV) extracts are able to improve the efficacy of prulifloxacin in bacterial prostatitis patients: results from a prospective randomized study. *Int J Antimicrob Agents* 2009 Jun; 33(6): 549-53


Nahata A, Dixit VK. Ameliorative effects of stinging nettle (Urtica dioica) on testosterone-induced prostatic hyperplasia in rats. *Andrologia* 2012 May; 44 Suppl 1:396-409


**Diindolylmethane (DIM), I3C**


Li Y et al. Selective growth regulatory and pro-apoptotic effects of DIM is mediated by AKT and NF-kappaB pathways in prostate cancer cells. *Front Biosci* 2005 Jan 1;10:236-43.


Tofovic SP et al. 2-Hydroxyestradiol attenuates the development of obesity, the metabolic syndrome, and vascular and renal dysfunction in obese ZSF1 rats. *J Pharmacol Exp Ther.* 2001 Dec; 299(3):973-77.

Wang TT et al. Broccoli-derived phytochemicals indole-3-carbinol and 3,3'-diindolylmethane exerts concentration-dependent pleiotropic effects on prostate cancer cells: comparison with other cancer preventive phytochemicals. *Mol Carcinogenesis* 2012 Mar; 51(3): 244-56


Zeligs MA. The cruciferous choice: diindolylmethane or I3C? Access at http://www.dimfaq.com/site/cruchoice.htm


**Vitamin D-3**


Penna G et al. The vitamin D receptor agonist elocalcitol inhibits IL-8-dependent benign prostatic hyperplasia stromal cell proliferation and inflammatory response by targeting the RhoA/Rho kinase and NF-kappaB pathways. *Prostate* 2009 Apr 1; 69(5): 480-93


**Cranberry (fruit extract)**


Howell AB, Foxman B. Cranberry juice and adhesion of antibiotic-resistant uropathogens. *JAMA* 2002 Jun 19; 287(23): 3082-83


University of Maryland Medical Center: [http://www.umm.edu/altmed/articles/cranberry-000235.htm](http://www.umm.edu/altmed/articles/cranberry-000235.htm)


**Saw Palmetto Extract (Serenoa repens, (fruit))**


Baron A et al. Sereona repens extract targets mitochondria and activates the intrinsic apoptotic pathway in human prostate cancer cells. *BJU Int* 2009 May; 103(9): 1275-83


Pais P. Potency of a novel saw palmetto ethanol extract, SPET-05, for inhibition of 5 alpha reductase II. *Adv Ther* 2010 Aug; 27(8): 555-63


University of Maryland Medical Center: [http://www.umm.edu/altmed/articles/benign-prostatic-000018.htm](http://www.umm.edu/altmed/articles/benign-prostatic-000018.htm)
Zinc


