

# The Holistic Approach to Prostate Health

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**Note from the editors:** Prostate cancer is the most common cancer, other than skin cancers, in American men and is the second-leading cause of cancer death in this group. The American Cancer Society estimates that during 2007 some 218,890 new cases of prostate cancer will be diagnosed in the United States and 27,050 men will die from it—accounting for about 10% of cancer-related deaths in U.S. men. About 1 man in 6 will be diagnosed with prostate cancer during his lifetime, but, at current rates, only 1 man in 34 will die of it. A little more than 1.8 million men in the United States are survivors of prostate cancer.<sup>1</sup>

Considering the importance of this topic, IMCJ is pleased to provide insights and information from one of the leading researchers in the area of prostate health. This article contains excerpts from Dr. Katz' Guide to Prostate Health: From Conventional to Holistic Therapies by Aaron E. Katz, MD (Excerpt 1, p. 39-53; Excerpt 2, p.150-164). Reprinted with permission from the publisher, Freedom Press (Topanga, Calif).

The holistic approach to prostate health attempts to correct underlying conditions through many different modalities. It involves diet, nutritional habits, natural medicines, lifestyle, stress levels, exercise, and personal hygiene. Men in other parts of the world, particularly Europe, commonly use natural medicines and successfully avoid prostate surgery and drugs. Even mainstream urologists are starting to hear about these therapies, because the science is sophisticated and the results are impressive.

Why haven't you heard more about these therapies, then? Because these natural medicines, which cannot be patented, simply aren't profitable enough to the large drug companies. Since drug companies can't make big profits on natural substances, they don't put the money into the research or the advertising necessary to put a natural medicine on the map.

Doctors who want to know more about natural medicines have to do their own homework—not an easy task when added to the huge amount of allopathic research in which they are expected to stay current, not to mention learning how to do new procedures or finding out about new drugs. The allopathic community is only just beginning to embrace alternative medicine (herbs, nutrients) rather than expeditiously shunning any colleague who dares suggest that roots and leaves might be medicine every bit as good as chemical pharmaceuticals.

## The Safe and Natural Pathway to Prostate Health

In recent years, mainstream medicine has rediscovered the wisdom of ancient healers, proving that the efficacy and safety of many traditional, natural remedies can easily stand up to the

rigors of controlled trials. Plant medicines, long used by native healers to treat genitourinary problems, are being discovered by modern science.

You can put these botanical medicines from nature's pharmacy to work for you. Recent evidence of their power to maintain prostate health has been demonstrated in clinical trials, and has demonstrated activity similar to the 5 alpha-reductase inhibitors or alpha-blockers. Generally, men show improvement, although it may take weeks to months for supplements to "kick in" and yield benefits. I have yet to see a man experience unpleasant side effects from the herbs discussed below.

## Herbal Remedies

### Saw Palmetto Berry Extract

One important healing herb that should be in a natural men's support formula is *Serenoa serrulata sabal*: the saw palmetto berry. Saw palmetto is a dwarf palm that grows to be 6 to 10 feet tall, and can be found in sandy, wind-swept coastal areas of the southeastern United States, especially Florida, Louisiana, Georgia, and South Carolina.

Native Americans have long used saw palmetto as an invigorating tonic for the entire genitourinary system. In 1892, an article by A. L. Marcy appeared in the *American Journal of Urology*. The author noted that 9 of 10 men eventually will suffer an enlarged prostate, and that saw palmetto had been proven especially effective in treating this problem.

In my own urological practice, I prefer to start patients with minimal lower urinary tract symptoms with saw palmetto. For example: If the patient is just starting to notice that his stream has diminished, or perhaps he is getting up one to two times per night, he would be an ideal patient to start with herbals rather than medications. In cases where the symptoms worsen, and the patient is experiencing more discomfort, I add medicines like Proscar and an alpha-blocker (Flomax or Uroxatral). In rare cases where these combinations do not help, or there is bleeding from the prostate, I recommend surgery—minimally invasive, if possible.

Medicinally, the most important part of the plant is its wrinkled, oval-shaped, red-brown berries. This powerful plant's effectiveness in the treatment of BPH has been extensively studied by the modern European medical community, with favorable results. Use of this plant extract has been shown to be effective in terms of improving urinary flow rate and decreasing residual urine volume. Moreover, *Serenoa serrulata* is effective over extended periods of time.

Saw palmetto works in a manner similar to that of finasteride, inhibiting the enzyme responsible for the formation of DHT and preventing uptake of DHT by prostatic tissue. As for side

effects, there are none, and no known cases of drug interactions.

The authors of a report in the Italian medical journal *Terapia Medica note*, “In view of the almost complete absence of side effects, the lack of [negative] changes produced in terms of sexual activity, and the clear improvement in [symptoms], we believe *Serenoa [serrulata]* to be a useful drug, and one which in particular should be adopted in the early phases of [enlarged prostate].”

### Buyer Beware

Keep in mind as you read on that a lot of companies are trying to make a quick dollar on this hugely popular herbal healer, but only a few are paying attention to producing a quality product that really works.

The amount generally recommended corresponds to the degree of standardization of the extract. In fact, if you don't purchase a broad-spectrum extract that provides the fatty acid fraction required for clinical efficacy, you may not get the results you expect.

The major studies on saw palmetto were all conducted using a specific concentrated extract form of the plant's berries. The berries are a rich source of oils, powerful fatty acids that have shown a remarkable affinity for the male genitourinary tract and for inhibiting excesses of the testosterone by-product DHT.

Saw palmetto works by:

- helping to rebalance the body's hormones and the ratio of testosterone to DHT;
- reducing the body's concentration of DHT;
- interfering with DHT's binding to prostate tissue;
- inhibiting alpha receptors, a mechanism similar to that of the alpha-blocker drugs currently prescribed, without the side effects caused by those medications.

As a result, the patient's prostate may shrink back to a presumably more youthful state, reducing blockage of the urethra and eliminating symptoms of enlarged prostate without surgery or medical drugs.

Saw palmetto is an herbal remedy that holds great promise for men. Currently, the NIH is about to initiate a large clinical trial in the United States to determine the efficacy and safety of this compound alone, and in combination with another herb, *Pygeum africanum*. The results of this study may not be available for several years. If you hear about this study in your community, I would urge you to participate if you meet the entry criteria.

I've seen saw palmetto work again and again. Within two months, about 70 percent of my patients respond favorably. This natural healer has saved many of my patients from having to use prescription medicine or undergo surgery. Standardized

saw palmetto has no known drug interactions; this has been demonstrated in a large number of well-conducted studies. I can say with complete assurance that saw palmetto is totally safe.

### Pygeum africanum

In the 1990s, the natural medicine *Pygeum africanum* arrived in the U.S. It has long been a popular natural remedy for prostate enlargement in France, and it is well validated by current science. At the Center for Holistic Urology, men who have been doing their own research into natural remedies often ask whether they should use saw palmetto berry extract, *Pygeum africanum*, or both.

*Pygeum africanum* is derived from the bark of an African evergreen tree, growing to a height of more than 100 feet. This species of tree is found on the high-elevation plateaus of southern Africa, the island of Madagascar, and in Central Africa, particularly in Cameroon and Kenya. Scientific evidence from European studies shows that *Pygeum africanum* consistently and reliably reduces symptoms of BPH.

Other evidence suggests that pygeum inhibits prostate cell proliferation that is at the root of both BPH and prostate cancer. The positive effects of pygeum have been found to last for at least one month after stopping its use. Medical studies indicate that pygeum may improve fertility in cases in which diminished prostatic secretion plays a significant role. Specifically, when men with diminished prostatic secretion use pygeum regularly, the volume of seminal fluid in their ejaculate increases. So do proteins in the semen that help nourish sperm.

A 1991 double-blind study conducted by Italian investigators indicates that men with either BPH or prostatitis who use pygeum may enjoy better, stronger erections. Pygeum also appears to enhance and renew sexual vigor by acting as a tonic, improving the underlying health of the genitourinary system.

Pygeum appears to work by:

- inhibiting formation of hormones known as prostaglandins that are responsible for painful inflammation of the prostate;
- acting as a diuretic to relieve bladder pressure;
- and (possibly) by inhibiting absorption and metabolism of prostatic cholesterol, which some researchers suggest is part of the BPH pathology.

Pygeum has become one of the urologist's drugs of choice in France and other European nations. No interactions of pygeum with any drug have been reported. As researchers noted in a 1990 report, “Use of the extract of *Pygeum africanum* seems justified especially due to its extremely favorable benefit-risk ratio as part of drug therapy.”

#### A Note on Clinical Trials

Doctors rely on large, multicenter trials to prove that a medication or an herbal compound is safe and effective. This is the manner by which medications achieve FDA approval. For herbs, which do not require FDA approval, these standards do not have to be met. Herbal compounds can just appear on the shelf in the health food store. However, the only way that physicians in the United States will believe that herbs work will be from the results of large clinical trials. From my own experience, and reviewing the literature, I believe that the results will show that in the patient with mild symptoms, saw palmetto is safe, effective, and likely to be as good as the medications out on the market.

### ***Pygeum for Bladder Dysfunction***

Often accompanying BPH, bladder dysfunction is a major—but often overlooked—affliction associated with male aging. As men age, they often suffer severe, irreversible alterations in bladder function, including partial or complete obstruction. Researchers have identified major cellular changes in the bladder that result from such obstruction. These include progressive free radical-related damage to the nerves and cellular mitochondria (energy factories) of the bladder.

A recent experimental study from Albany College of Pharmacy, New York, shows that pretreatment with pygeum significantly reduced the severity of metabolic dysfunction associated with partial outlet obstruction. Hopefully, more research will be done to demonstrate the utility of pygeum in the prevention of bladder dysfunction in aging men.

### ***To Replace Saw Palmetto with Pygeum?***

The question many men will have is whether to replace saw palmetto extracts with pygeum as part of their daily prostate health regimen. These two herbs have slightly different modes of action, according to recent studies from research centers, such as the Department of Urology, University of Essen, Germany. Saw palmetto blocks the enzyme responsible for converting free testosterone to the toxic dihydrotestosterone (DHT) molecule. Pygeum works by enhancing prostatic secretions, acting as a diuretic, and decreasing inflammation. Nettle, another prostate-health herb that I'll discuss in the next section, has anti-inflammatory effects. Your wisest course of action might be to combine these herbs and cycle them, or take them together.

One study by Swiss researchers examined the interactive effects of pygeum and nettle root (see below) on the action of two enzymes involved in production of dihydrotestosterone and estrogen. (Increased ratio of estrogen to testosterone in elderly men has been linked with BPH.) In the lab, they found that both plant extracts effectively inhibited DHT and aromatase, the enzyme that transforms testosterone into estrogen. A combination of both extracts was significantly more effective than either extract alone at blocking the activity of aromatase.

### **More Great Natural Medicines for BPH**

Here are some other compounds you can look for in your herbal remedy. They all have varying degrees of scientific support, but all are backed by considerable traditional and anecdotal evidence.

**Nettle root.** The use of stinging nettle (*Urtica dioica*) has its origins in Indian medical history, where it was used to relieve the stinging, prickling sensations of prostate infection and enlargement. Some unpublished data indicate it could work by inhibiting 5 alpha-reductase, or by inhibiting the aromatase enzymes that convert testosterone to estrogen in the male body. Nettle root appears to work synergistically with *Pygeum africanum*.

**Flower Pollen.** Cernilton® is a flower pollen extract manufactured by Swedish company AB Cernelle. This natural medicine is made from cernitin, a mix of rye pollen from several different plants grown in the southern part of the country. It has

a relaxant effect on the smooth muscle that surrounds the urethra, and has been reported to slow the growth of prostate cells. Cernilton was introduced to the European market over 30 years ago and continues to be used as a first-line defense for patients with prostatitis.

In 1990, British physicians tested Cernilton's effectiveness in treating BPH-related impaired urine flow. Sixty patients were involved in the study, half receiving Cernilton and the other half placebo. After six months, 69 percent of the patients reported improvement in symptoms. Researchers also found a decrease in residual urine and prostate diameter.

In another study, 79 patients with BPH were treated with 126 mg of Cernilton three times a day for more than 12 weeks. Their symptoms included urinary flow obstruction, increased prostatic volume, and residual urine. Scientists reported that the extract produced a statistically significant improvement of 69 percent of the symptoms compared with an improvement of 30 percent with placebo. A decrease in residual urine volume and in prostate volume was observed.

Finally, in a Japanese study published in 1990, 192 patients were treated with Cernilton. After four weeks, moderate or great improvement was seen. Patients improved in terms of residual urinary volume, average urine flow rate, maximum flow rate, and prostate weight.

Cernilton is available at health food stores and natural product supermarkets throughout the country. There are no reports of toxicity tied to this product. However, some users may experience mild to moderate heartburn and nausea.

**Beta-sitosterol.** This compound is found in many of the plant foods we eat, including rice, soy, corn, wheat, and peanuts. It appears to help relieve symptoms in men with BPH. (It is also being studied as a natural remedy for high cholesterol, and as an aid to recovery from intense exercise.) One study found that when 200 men with BPH were given 20 mg of beta-sitosterol three times daily for six months, urinary flow and other symptoms improved significantly. The placebo group in this study demonstrated no improvement. In another double-blind study, 130 mg per day of beta-sitosterol yielded similarly encouraging results.

**Vitamin B<sub>6</sub>.** The intake of this B vitamin is commonly low; it is scarce in modern processed-food diets. Its scarcity poses a risk to the prostate because it—along with zinc, discussed below—is needed to create and maintain hormone balance and to make testosterone. More specifically, vitamin B<sub>6</sub> is needed to produce a substance called picolinic acid, which in turn is needed for the utilization and absorption of zinc, and to convert zinc into forms that the body needs. Both zinc and vitamin B<sub>6</sub> work together to rebalance the body's hormones and build testosterone.

**Zinc.** The secretions of the prostate gland contain an abundance of this mineral, which strongly suggests that zinc plays a role in prostate function. Zinc supplements have been found to help shrink the prostate and to relieve symptoms of BPH. The usual recommendation is 30 to 50 mg daily of zinc. In a study presented at a meeting of the American Medical Association, 19 men with BPH took 150 mg of zinc per day for

two months, then lowered their dosages to 50 to 100 mg per day; 74 percent of the men in this preliminary study experienced shrinkage of the prostate.

The research evidence that zinc alone is effective is not all that strong, and taking too much zinc can cause copper deficiency. Ensure that you are getting 2 to 3 mg of copper each day through a multivitamin and mineral supplement.

**Amino acids.** A combination of three amino acids (glycine, alanine, and glutamic acid) has been found to improve BPH symptoms. Men with BPH were given a total of approximately 760 mg of these amino acids three times daily for two weeks, after which their dosages were ramped down to 380 mg three times a day, with the therapy lasting three months total. Half of the subjects reported that they had less urinary urgency and frequency, and/or that they had less trouble starting the flow of urine. Only 15 percent of the placebo subjects reported improvements. Why would amino acids help? No one knows for certain, but they appear to shrink swelling of prostatic tissue.

**Pumpkin seeds.** The seeds of pumpkins and other winter squash, all members of the genus *curcubita*, were used by Native American Indians to heal prostate problems. In Europe today, pumpkin seeds are a widely used therapy for urinary symptoms of BPH and to calm overactive bladder. They are nutrient dense, containing protein, B vitamins, fiber, iron, manganese, copper, calcium, and magnesium. Interestingly, pumpkin seeds are also an effective natural remedy for intestinal parasites. They contain a unique amino acid called *curcurbitin*, which has been found to paralyze intestinal parasites so that they can be expelled by the body.

In countries where pumpkin seeds are eaten often, there is a lower incidence of prostate problems. It's believed that these seeds contain fatty acids that block the action of DHT on the prostate. You can eat pumpkin seeds raw, or toast them in the oven; or if pumpkin seeds aren't on your short list of favorite foods, you can take a supplement that contains concentrated pumpkin seed oil.

**Essential fatty acids (EFAs).** The importance of adequate essential fatty acid nutrition is becoming evident in a great many so-called "diseases of aging." Modern diets are very low in EFAs, or contain unbalanced amounts of these fats. The EFAs are transformed into hormone-like biochemicals in the body, and these biochemicals have enormous impact on inflammation, blood clotting, and a host of other processes that can dictate whether we're chronically sick or chronically well. Suffice it to say that proper fatty acid nutrition can help to reduce the size of the prostate by reducing inflammation.

Not much research has been published on the effects of EFA supplements on BPH. We do know that proper EFA balance promotes better heart and joint health; it may help to prevent allergies, autoimmune disease, and even some cancers. More research is needed, but in the meantime, getting more of the omega-3 fatty acids—those found abundantly in flaxseeds and fish—is helpful in so many ways that it won't hurt to add them to your prostate health regimen. Most experts recommend a tablespoon of flaxseed oil per day, or two to four tablespoons per day of ground flaxseeds. Ground flaxseeds have the added bonus

Herb/Nutrient	Dosage	Side Effects/Drug Interactions
Saw palmetto	60 mg Twice a day	Rarely, mild gastrointestinal upset or abdominal pain; dizziness and headache have been reported rarely; and in rare cases there may be decreased libido or male breast enlargement (the latter goes away when the supplement is stopped)
Pygeum	50 mg twice daily or 100 mg once daily	Possible gastrointestinal discomfort
Nettle root	300 to 600 mg extra twice a day; especially good combined with pygeum	Mild gastrointestinal upset, diarrhea; take with food to prevent this; rash if the extract is applied topically—which you should never do
Cernilton	126 mg three times day	Possible gastrointestinal discomfort
Beta-sitosterol	20 mg three times a day	Rarely, mild gastrointestinal upset
Vitamin B	50 mg daily	none reported
Zinc	30 to 50 mg daily (make sure you also get 2 to 3 mg copper)	Immune system suppression with long-term doses over 100 m
Amino acids: ciglycine, alanine, glutamic acid	380 to 760 mg three times a day	Not advisable in men with kidney disease; otherwise, no adverse effects reported
Pumpkin seed oil	160 mg three times per day, with meals	None reported
Essential fatty acids	Choose a supplement that gives you 600–1,000 mg per day of the omega-3 fatty acids EPA, DHA, and/or ALA; fish oil should come from Arctic fish (salmon, sardines); any EFA supplement should also contain an herbal or antioxidant vitamin preservative (e.g., vita- min E, rosemary)	Fish oils may have a fishy repeat if taken without food; consult your doctor if you are on any kind of blood-thinning drug, including aspirin

of being high in beneficial fiber.

Fish oil is an excellent source of EFAs; choose oils from deepwater fish, such as salmon, sardines, or anchovies, and aim

for a dosage of about 600 to 1,000 mg of omega-3 fats per day. If you do add extra EFAs to your diet, also add a vitamin E supplement (200 IU daily).

**Exercise.** A higher level of physical activity appears protective against BPH. A study published in the *Archives of Internal Medicine* found that men who did more physical activity had decreased likelihood of BPH symptoms, diagnosis, and surgery. Men who walked for two to three hours per week lowered their risk of BPH by 25 percent compared to men who did not exercise.

### **When to Use Additional Herbs and Nutrients** **Our Best Advice from the Center for Holistic Urology**

There is no question that remedies like saw palmetto and pygeum have a place for men with BPH. Many men can gain big benefits from herbal remedies. However, each person is different, and different herbs and nutrients bring with them specific qualities that may help an individual. Give these formulas for a few months and keep track of your urinary symptoms. If your frequency has diminished, your urine stream grown stronger, and congestion declined, then the product may be all that your system requires.

Start with saw palmetto berry. If additional help is required, use nettle, pygeum and pumpkin to augment your saw palmetto supplement. Take three to four capsules daily to achieve the therapeutically proven dosage for pygeum (which is 100 mg daily).

If you feel that your symptoms are about the same or only showing slight improvement, then you should next combine ingredients in various formulas. For example, another formula that many of my patients like combines nettle with pygeum and pumpkin.

### **Other Holistic Therapies for Men with Prostate Cancer**

The use of unconventional herbal therapies (phytotherapies) for prostate cancer as well as for other malignancies has been dramatically rising in the last few years in the United States. A survey conducted in 1990, focusing on the use of alternative treatments for cancer, estimated that there were 425 million visits to providers of unconventional therapies during the previous year, and that the expenditures associated with this use amounted to approximately \$13.7 billion. It is likely that these numbers have increased since that time. Here, I intend to help you to avail yourself of the best that these unconventional therapies have to offer, should you be in the unfortunate position of needing them.

You can use substances from nature to support your immune system, increase energy levels, improve your body's native ability to squash cancer cells, and control side effects from treatment. If you are fortunate enough to have a small, slow-growing cancer that is being watched carefully without being treated, you are a perfect candidate for holistic therapy. And if you do not have prostate cancer but wish to hedge your bets against ever having it, many of the herbs and nutrients we recommend at the Center will be useful to you. In this section, I'll talk about medicinal mushrooms, curcumin, lycopene, antioxi-

dants, IP<sub>6</sub> and soy for prostate cancer patients. You will also learn about more supplements for reducing inflammation, a key player in prostate cancer progression, and about the usefulness of acupuncture and support groups for men with this disease.

### **Frankincense (*Boswellia serrata*)**

This herb, derived from the gummy sap of the boswellia tree, has been used in Ayurvedic medicine for centuries, primarily to treat illnesses related to excess inflammation (arthritis, ulcerative colitis, Crohn's disease, asthma). Modern research has traced its medicinal effects to active constituents called *boswellic acids*.

Boswellia studies show that this herb powerfully inhibits 5LO activity and that it blocks the formation of both 5-HETE and leukotriene B<sub>4</sub>. If you would like to try boswellia, take 200 to 400 mg, three times daily, of a standardized extract that contains between 37.5 and 65 percent boswellic acids.

### **Medicinal Mushrooms**

Mushrooms contain a wide variety of unique *polysaccharides*, complex carbohydrate molecules that have notable antitumor and immunostimulant properties. They appear to be useful not only in oncology—for their apoptosis-inducing, tumor-shrinking, anti-inflammatory, and side effect-reducing properties—but in other fields of medicine, as well. They improve immune function, cardiovascular health, liver function, and blood sugar balance, and have been used to enhance energy levels and even sexual performance.

Medicinal mushroom compounds have clear value for the prevention and treatment of many of the health conditions that have stumped modern medicine. Active Hexose Correlated Compound (AHCC) and Genistein Combined Polysaccharide (GCP), both derived from medicinal mushrooms, are currently the subject of much research attention.

### **Active Hexose Correlated Compound (AHCC)**

This compound is derived from cultivation and enzymatic modification of several species of mushroom mycelia, including shiitakes. In Japan, AHCC is considered to be a "superfood," and the research into its application to cancer therapy is promising—particularly when it is used in combination with GCP. Its effects on breast cancer and liver cancer growth have been the most researched up to this point.

Studies suggest that AHCC works against cancer growth in a number of ways. It appears to increase the activity of natural killer (NK) cells and macrophages, and it also may improve liver function and act as an antioxidant. AHCC also shows promise as an adjuvant therapy for patients undergoing chemotherapy, helping to reduce nausea, pain, vomiting, loss of appetite, liver damage, and immune suppression. It is likely that further research will show AHCC to be a valuable adjunctive therapy for prostate cancer.

### **Genistein Combined Polysaccharide (GCP): Combining Soy with Mushroom Phytochemicals**

Research into GCP has suggested that this supplement

fighters prostate cancer by reducing blood flow to the tumor (antiangiogenic effects); by enhancing apoptosis of cancerous prostate cells; and by increasing tolerance to chemotherapy and radiation. It is antiangiogenic both in vitro and in vivo. And lab experiments have shown GCP to have greater activity than genistein alone. Test tube studies at Columbia and elsewhere have shown growth inhibitory effects on prostate and breast cancer cells with GCP.

Epidemiological reports (large-scale studies that compare disease incidence in various populations and search for possible reasons for those differences, such as differences in diet) suggest that Asians consuming a diet high in soy have a low incidence of prostate cancer. Soy and one of its principal constituents, genistein, have been demonstrated to suppress the development of prostate cancer in experimental studies.

Overall, the research suggests that genistein is nontoxic and that it strongly protects against prostate cancer, primarily via inhibition of a signaling pathway required by cancerous cells to proliferate. Numerous studies have shown that soy isoflavones (including genistein and daidzein) inhibit the growth of prostate cancer in mice, and consistently alter measurements and markers associated with prostate cancer growth—including angiogenesis, the growth of blood vessels to feed the tumor. Genistein Combined Polysaccharide (GCP; Amino Up Chemical Co., Sapporo, Japan) is sold as a nutritional supplement in Japan, the United States, and other countries. It is prepared by fermenting soy extract with mushroom mycelia. This process increases the bioavailability of soy isoflavones, the compounds believed to be responsible for the chemopreventive effects of soybeans and soy-containing foods. Our laboratory has published data showing GCP has a dose-dependent growth inhibitory effect on prostate and bladder cancer cell growth in vitro. In fact, we found that GCP was more effective in inhibiting cancer cell growth than pure genistein, the major soy isoflavone. The manufacturers report a study where two grams per day of GCP were given in pill form to 27 healthy human volunteers for 28 days. Blood tests were done before the trial began and on days 14 and 28 (liver enzymes, blood sugars, cholesterol, triglycerides, nitrogen levels, and other blood measurements used to discern whether a drug is toxic), and all were within normal limits. In our experience at Columbia, the most common complaint in those who use this supplement is flatulence.

At Columbia, we wrote up a case study for the *Journal of Alternative and Complementary Medicine* about a patient who had significant regression of his prostate cancer following the use of GCP. The patient was enrolled in a study where he received GCP for six weeks prior to radical prostatectomy. After 44 days of low-dose GCP, the patient's PSA fell from 19.7 to 4.2. More strikingly, after the radical prostatectomy was performed, there was no identifiable cancer in the gland. The patient complained of no side effects.

More research is forthcoming. We instruct patients on a watchful waiting protocol to take five grams of GCP daily. Unfortunately, GCP is very expensive, in the range of \$275 to \$600 for a month's supply.

### Vitamin D for Metastatic Prostate Cancer

Several studies show a link between sun exposure—more specifically, exposure to UVB rays and the vitamin D formation that is stimulated in skin by those rays—and reduced risk of and mortality from prostate cancer. Men with genetic variations that decrease their vitamin D levels are at increased risk of developing the disease. This could help to explain why African Americans, whose dark skin does not absorb as much UVB radiation, are at increased risk compared to Caucasians. Men who live in colder climates and get less sun are also at increased risk.

The mechanism is still being studied, but it appears to have something to do with the influence of vitamin D levels on a substance called insulin-like growth factor 1 (IGF-1).

Patients with advanced, hormone-refractory prostate cancer often develop a deficiency of vitamin D. In a study published in the *Journal of Urology*, researchers evaluated the effects of 2,000 IU of vitamin D per day, administered to men with metastatic, hormone-refractory prostate cancer for 12 weeks. At each four-week increment, patients filled out questionnaires designed to evaluate pain and muscle strength, and had their blood calcium and vitamin D levels measured. Of those treated with vitamin D, four patients (25 percent) had improved pain scores; six (37 percent) had improvements in muscle strength. Vitamin D may turn out to be a valuable natural therapy to help men with advanced disease to control pain, maintain strength, and improve their quality of life. More research still needs to be done to find the optimal dosage, and to find out whether vitamin D supplements might help men who are in earlier stages of prostate cancer.

Getting extra vitamin D by drinking milk may not be the best plan. Research from the Harvard School of Public Health shows that men who consume more milk (more than four glasses a day) have lowered vitamin D levels. Dietary calcium “uses up” vitamin D. Although vitamin D is added to milk, it is not enough to make up for its high calcium content.

Get extra vitamin D through regular exposure to sunlight (15 to 30 minutes, three times a week, if possible), without sunscreen. If you live in a climate where this is not possible, use a multivitamin that contains up to 400 IU per day of vitamin D.

### Still More Nutrients for Prostate Cancer Prevention

**Lycopene.** This is a carotenoid nutrient that lends red color to fruits and vegetables. It is most often associated with tomato products, because 80 percent of the lycopene consumed by the average person comes from foods like tomatoes, tomato sauce, and ketchup. In studies of populations with varying amounts of lycopene in their diets, an association has been found between high lycopene consumption and low risk of prostate cancer. Men with prostate cancer have lower levels of this nutrient in their bodies. Taking lycopene supplements has been found to slow the growth of tumors and lower PSA scores in men with prostate cancer. Cooked tomato products contain more bioavailable lycopene. It appears that tomatoes cooked with oil are the best source of this nutrient.

**Vitamin E.** In a study of mice implanted with human prostate tumors, it was found that the growth-promoting effects

of a high-fat diet were curbed by vitamin E. In one large Finnish study, reported in the *New England Journal of Medicine*, vitamin E was shown to be highly protective against prostate cancer. All men should take a minimum of 240 IU of vitamin E daily. New research suggests that more vitamin E is not better; an analysis of studies on this nutrient found increased heart failure in people who took high doses (above 400 IU per day). Choose a version that contains the d-alpha tocopherol succinate form of vitamin E.

**Selenium.** This trace mineral is essential for life. It works as an antioxidant alongside vitamin E, cooling the fires of excess oxidation. The amount obtained in the diet can vary widely due to variations in selenium content of soil in different parts of the world where food is grown. Population studies consistently show that men with higher intake of selenium have lower risk of cancer of the prostate, and that men with prostate cancer have lower selenium levels than men without it.

The protective effects of selenium against cancer—and not just cancer of the prostate—are remarkable. One study at the Arizona Cancer Center at the University of Arizona in Tucson was designed to measure the effects of 200 mcg per day selenium supplementation versus placebo on cancer risk. Here's what they found:

- There was a slight reduction in risk of death from all causes in the selenium group: 108 deaths in the selenium group and 129 in the control group.
- There were highly significant\* reductions in deaths from cancer. The selenium group had 29 deaths from cancer during the follow-up, and the control group had 57.
- The selenium group had 77 cancers, and the control group had 119 cancers. The risk of prostate cancer was decreased by nearly 60 percent.

These results were so promising that the control arm of the trial was stopped early, to give the control subjects a chance to take advantage of this powerful nutritional therapy. It's important to note that the University of Arizona researchers used a special form of selenium derived from fermented yeast. Fermentation is achieved by adding a yeast called *Saccharomyces cerevisiae* to selenium salt. The yeast biotransforms the selenium, making it more biologically active and exerting enhanced anti-cancer activity. At this writing, the Arizona researchers were well into a second series of studies on selenium.

The SELECT (selenium and vitamin E chemoprevention trial) study, which is currently underway, builds on previous evidence that supplementing men with these two nutrients over several years' time will cut their risk of prostate cancer substantially. The 12-year, government-sponsored study involves 32,400 men at about 300 research centers in the United States and Canada. It will be the largest prevention trial ever undertaken using a drug or nutrient.

In one study published in the *British Journal of Cancer*, the

authors concluded that the selenium treatment was associated with a 63 percent reduction in prostate cancer recurrence in 974 men with a history of the disease.

**Vitamin C.** Several studies have found an inverse relationship between blood vitamin C levels and cancer; in other words, the higher the vitamin C levels, the less likely the person is to have cancer. One study found that vitamin C slowed cell division and cell growth in two androgen-independent prostate cancer cell lines. A study by another research group found that men who had higher dietary vitamin C intakes had better odds for survival when they developed prostate cancer.

**IP<sub>6</sub> with inositol.** Inositol hexaphosphate (IP<sub>6</sub> with inositol) is a nutrient found in soy, rice, sesame, legumes, beans, corn, and whole grains. IP<sub>6</sub> with inositol has shown strong inhibitory action against prostate cancer.

In 1995, University of Maryland researchers investigated the effects of inositol hexaphosphate on growth inhibition and differentiation of human prostate cancer cells PC-3 in vitro. When cells begin to differentiate again, it is a sign of a return to normal. A significant dose- and time-dependent growth inhibition was observed. A marker for prostatic cell differentiation, prostate acid phosphatase, was significantly increased after 48 hours of treatment. The compound "strongly inhibits growth and induces differentiation in human prostate cancer cells," said the researchers.

IP<sub>6</sub> enhances natural killer (NK) cell activity. NK cells are immune cells produced in the bone marrow. Once released into the bloodstream, they recognize and destroy both viral and cancer cells. In investigations of the effect of IP<sub>6</sub> on experimental NK cell activity, researchers found that a colon carcinogen called DMH depressed NK cell activity, but that treating the cell cul-

#### Antioxidants May Prevent Progression of PIN

Mitchell C. Benson, M.D., Ihor S. Sawczuk, M.D., urology resident David R. Knowles, M.D., and I recently evaluated the effects of selenium, lycopene, and vitamin E on the progression of PIN to prostate cancer. We followed 60 patients diagnosed with PIN from May 1993 through July 2000. The patients were advised to start a daily antioxidant therapy regimen, including 400 IU of vitamin E, 200 micrograms of selenium, and 20 mg of lycopene. Thirty-nine of the 60 patients—65 percent of the subjects—have, at this writing, undergone at least one repeat biopsy. Prior to each set of biopsies, free and total PSA was measured and PSA velocity calculated. Of the 39 re-biopsied patients, only 11 (28.2 percent) were diagnosed with prostate cancer. The average time to diagnosis of prostate cancer from the first PIN diagnosis was 14.9 months. The average follow-up for patients from first PIN biopsy to last benign biopsy was 21.1 months. These findings to me suggest that these antioxidants are working in the prostate gland to prevent the development of cancer, and should also be included in your daily regimen if you have a diagnosis of PIN.

\* This means that there is a statistical probability that the difference in cancer incidence between the selenium group and the control group could have been due to chance rather than to the supplement. When the results of a study are said to be significant, we mean that the results were most probably not due to chance—that they were caused by the intervention.

ture with IP<sub>6</sub> reversed the NK cell depression. IP<sub>6</sub> also enhanced the potency of the NK cells, with higher doses of the nutrient bringing about greater cancer cell-killing activity.

More recent research on IP<sub>6</sub>, performed at the Department of Pharmaceutical Sciences at the University of Colorado Cancer Center, involved mice inoculated with hormone-refractory prostate cancer cells that were then given either plain drinking water or water containing 1 or 2 percent IP<sub>6</sub> for 12 weeks. The volume of tumor growth was suppressed in the animals given IP<sub>6</sub>, in the mice who got the higher dose of the nutrient, by 66 percent. In mice who got only 1 percent IP<sub>6</sub> in their water, tumor volume was reduced by 40 percent compared to the mice who got plain water. When the tumors were examined, the researchers found increased apoptosis in those from IP<sub>6</sub>-fed mice, and decreased markers of uncontrolled, undifferentiated cellular growth and markers of angiogenesis.

IP<sub>6</sub> with inositol is a formula that every American should consider because it has such a wide spectrum of action against cancer.

**Saw palmetto.** In a recent clinical study, saw palmetto was found to inhibit conversion of testosterone into the toxic metabolite dihydrotestosterone (DHT) and to lower levels of epidermal growth factor (EGF), a key driver of cancerous cell growth, while enhancing men's levels of beneficial free testosterone. High levels of both DHT and EGF have been suggested to play a role in prostate cancer.

**Beta-sitosterol.** Phytosterols like beta-sitosterol are used widely in Europe to treat enlarged prostate (BPH). Beta-sitosterol is a minor component of saw palmetto and pygeum, both herbs that support prostate health. Nutrition researchers at the University at Buffalo have provided the first evidence that this phytosterol appears to play a role in inhibiting the growth of human prostate-cancer cells, according to Atif Awad, Ph.D., head of the University of Buffalo's Nutrition Program, in a presentation on October 25 at the Sixth International Conference of Anti-Cancer Research in Kallithea, Greece. They found that the phytosterol B-sitosterol, a fat abundant in vegetarian diets, enhances an intracellular signaling system that tells cells not to divide. The study showed a 28 percent inhibition of prostate-cancer cell growth after being exposed to B-sitosterol for only five days. The authors write, "If cell proliferation can be stopped before it becomes uncontrolled, cancer can be contained. When we treated prostate-cancer cells with phytosterols, cell proliferation was inhibited."

The work of Awad and colleagues is grounded in epidemiologic studies showing that prostate cancer is less common in Asian countries, where diets are primarily vegetarian, and that rates increase when these people migrate to Western societies where rates are higher and diets are primarily animal-based.

### Lignans for Chemoprevention

We all know dietary fiber is a good thing. Adequate fiber helps with what is delicately referred to as "regularity," and we all know that a little regularity in the morning can make a big difference in the way your day goes. Soluble fiber, a type of fiber that is absorbed into the bloodstream through the intestinal wall, is known to help reduce "bad" LDL cholesterol levels in the

## Two Novel Plant Extracts Show Activity Against Prostate Cancer

By Vonalda M. Utterback, CN

Other promising approaches to prostate health have been under investigation at the Department of Urology, College of Physicians and Surgeons, Columbia University Medical Center in New York. Researchers have been exploring the anti-cancer effects of powdered extracts from Pao pereira and Rauwolfia vomitoria. The bark of P. pereira, a tree that grows in the Amazon rain forest, and the root of R. vomitoria, an African shrub, have rich histories of use by indigenous peoples and are also high in B-carboline alkaloids—natural compounds shown to have certain anti-cancer activities in a variety of cell lines.

A recent in vitro and mice in vivo study published in the International Journal of Oncology was conducted by the Columbia research team—led by Debra L. Bemis, PhD, and including Aaron Katz, MD. The study confirms anti-prostate-cancer activity for R. vomitoria extract. Findings show the herb significantly suppressed growth and progression of the androgen-dependent prostate cancer cell line NLCaP.<sup>1</sup> A second in vitro and in vivo study, this time on P. pereira, is due to be published by the team in late 2007.

Prior to their first published study, the Columbia team conducted extensive in vitro and in vivo preclinical studies on P. pereira and R. vomitoria as they relate to prostate cancer cells. The group has built on the extensive work of the late French biochemist Mirko Beljanski, who demonstrated that alkaloids from these plants selectively destroyed cancer cells in both mice and human cancer cell lines while sparing normal cells.<sup>2,12</sup>

The Columbia group's experiments suggest the two extracts exert their anti-cancer effects by different mechanisms of actions, with P. pereira inducing apoptosis, whereas R. vomitoria induces cell-cycle arrest. There is hope that combining the two herbs will produce a synergistic effect, so the combination is currently being tested in a Phase 1 clinical trial for men with elevated prostate specific antigen levels who are at relatively high risk for developing prostate cancer.

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body—one reason why you might have been inspired to start eating Cheerios again after a long hiatus. And chances are good that if your diet is fiber-rich, it's also rich in other good things like vegetables, whole grains, fruit, and legumes.

There is yet another health-promoting aspect to increasing your fiber intake. I'm referring to a specific type of fiber that has some other intriguing qualities that make it an ideal addition to a prostate cancer chemoprevention program: lignans.

The richest food source of lignans is flaxseed, although many other plant foods (seeds, whole grains, legumes, fruits,



and vegetables) contain small amounts. The research suggests that at least some of the benefits of including flax in your diet have to do with the way these lignans act once they've entered your body. Flaxseed is transformed by "friendly" bacteria in the intestines, turning substances in those seeds—known as lignan precursors—into natural chemicals called enterodiol and enterolactone. Enterodiol and enterolactone are phytoestrogens, like the genistein found in soy. They have the ability to bind to estrogen receptors throughout the body, blocking the binding of stronger estrogens to those sites.

When you're a young buck, testosterone rides herd over estrogen; but as you age, testosterone production wanes and estrogen production (through aromatization, a process where testosterone is transformed into estrogens in fat cells) doesn't. That excess estrogen has been implicated in both BPH and prostate cancer. Increasing lignans in the diet increases levels of phytoestrogens in the body, which, in turn, blocks the binding of excess estrogens to receptors in the prostate. Additionally, lignans may help to block the action of aromatase, the enzyme that transforms testosterone into estrogen, and of the enzyme that transforms testosterone into that enemy of the prostate gland (and the hairline), DHT.

At this writing, much research into the chemopreventive potential of lignans is going on. In a 1997 article published in the *Journal of Progressive Drug Research*, the authors write that lignans "have now been shown to influence not only sex hormone metabolism and biological activity, but also intracellular enzymes, protein synthesis, growth factor action, malignant cell proliferation, differentiation, and angiogenesis, making them strong candidates as natural chemopreventive compounds." Let's talk about some of the research that backs up these promising applications for lignans.

**Populations with high-lignan diets may have lower rates of hormone-dependent cancers.** In a study performed in Sweden, subjects with the lowest blood levels of enterolactone had increased risk of prostate cancer. Diets high in lignan-rich foods have been repeatedly associated with decreased risk of prostate cancer. Other research has suggested that high intake of lignans correlates with lower incidence of breast, ovarian, and uterine cancers.

**Flax supplementation slows the growth of prostate cancer between diagnosis and surgery.** In a study from Duke University Medical Center, researchers added flax to a low-fat diet prescribed to 25 patients scheduled for prostatectomy. The diet was 20 percent fat and supplemented with 30 grams of flaxseed a day.

The results were remarkable. Men who adhered to the diet for an average of 34 days (actual adherence ranged from 21 to 77 days) saw their total cholesterol drop an average of 25 points. Their testosterone and free androgen levels fell—a good thing when you're trying to control prostate cancer growth. More importantly, proliferation rate and apoptosis, in addition to other markers of cancer growth, were favorably altered by the low-fat/flax intervention.

Other studies have come to similar conclusions, with flaxseed helping to slow cancer growth in patients with prostate and breast cancers.

**Test-tube studies and animal studies show that lignans have anticancer effects.** In lab studies, lignans and their metabolites (enterodiol and enterolactone) have been found to increase apoptosis, downregulate the expression of sex steroid receptors (translation: reduce the cancer growth-enhancing effects of sex hormones in the prostate), and inhibit the growth of both androgen-dependent and androgen-independent prostate cancer cell lines. In animals with prostate cancer that has been experimentally caused, lignan supplementation slowed cancer growth. Lignans have been found to inhibit angiogenesis, the growth of extra blood vessels to feed hungry tumors. Lignans have antioxidant activity; they limit the activity of an enzyme associated with retroviral cancer-causing genes; and they inhibit the binding of estrogens to alpha-fetoprotein, a protein that is associated with cancer development.

### Increasing Your Lignan Intake

The evidence in favor of lignans supports adding ground flax to your diet. Purchase the whole seeds and keep a coffee grinder for flaxseeds only. Grind a tablespoon and add it to your yogurt, smoothie, or hot cereal; stir a tablespoon into soup or stew; add it to nut butters or other spreads. Aim for three tablespoons a day. You can also purchase a quality, pre-ground flaxseed product. And eat plenty of other nuts, seeds, vegetables, and legumes.

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