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# Prostate Forum

Solving the Puzzle

LETTER

Omega 3 Fatty Acids and Saw Palmetto

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# **Prostate Forum**

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### KEY POINTS

DHA plays an important role in the function of the brain and eyes.

Omega 3 fatty acids DHA and EPA, found in fish and fish oil, lower cholesterol, moderate high blood pressure, suppress inflammation and may reduce prostate cancer risk.

Omega-3 fatty acid ALA is associated with increased risk of metastatic prostate cancer. ALA can be converted to DHA and EPA, but the human body does so inefficiently.

ALA supplements yield a much greater increase in blood and tissue ALA for a relatively minor increase in DHA and EPA.

Neuromins, a DHA supplement extracted from cultivated algae, provides sufficient omega-3 fatty acids without the dangers of ALA or the risk of contamination.

Saw Palmetto extracts relieve the symptoms of benign prostatic hyperplasia.

Active extracts of saw palmetto inhibit conversion of testosterone to dihydrotestosterone, block formation of inflammatory compounds by 5-lipoxygenase, and block the action of prolactin and estrogen on prostate tissue.

Omega 3 Fatty

Acids:

What's New?

Saw palmetto extract brands vary widely in quality. Which one is best?

Readers of this newsletter have followed the evolving controversy over omega-3 fatty acids. Concern about omega-3 fatty acid intake has increased in response to clinical evidence supporting the ability of these fats to lower choles-

terol, moderate high blood pressure, and suppress inflammation associated with rheuma-

toid arthritis and other diseases. Many dietitians, as well as other health care professionals, recommend that patients increase their intake of ALA to ensure a sufficient amount of omega-3 fatty acids are consumed. Large concentrations of this fatty acid are found in flaxseed oil, where it comprises 50% of the total fatty acids. Canola and soy bean oil are also rich in ALA.

There have been six studies examining the impact of ALA on prostate cancer; five studies showed an adverse outcome associated with increased consumption of this fatty acid. The clinical studies were matched with laboratory

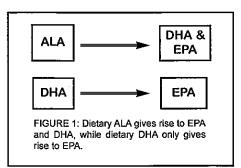
research that shows an increased growth of prostate cancer cells when exposed to ALA. We last reviewed flaxseed

oil and ALA in the February 2000 (5:2, pp. 7-8) issue. The article is now on our web site (www.prostateforum.com).

ALA is not the only omega-3 fatty acid (see Figure 1). Two others, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are found in the fat of ocean fish such as wild salmon or haddock. Fish do not

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from the algae they ingest. Farmraised salmon are usually fed corn or soy meal rather than algae; therefore, the fat in farm raised fish may not differ significantly



from the fat found in cattle or pigs fed a similar diet. Oil obtained from wild fish appears to have all of the same health benefits of ALA but is not associated with an increased risk of prostate cancer. In fact, several studies suggest a decreased risk of prostate cancer in men who eat several servings of wild fish a week.

We eat a low-fat vegan diet and recommend this for optimum results. Often in our travels. Rose and I found ourselves in situations where vegan options were not available. Under these circumstances, we ate wild salmon DHA is critical in instead. However, I have reservations about the use of either fish oil or fish as a source of omega-3 fatty acids. For more than a century, industrialized countries used the oceans as garbage dumps. There is a sizeable amount of literature documenting the toxic chemicals that concentrate in ocean fish. These chemicals range from heavy metals like mercury to other dangerous chemicals such as dioxin.

DHA, free of ALA and from sources not likely to be contaminated by outside influences, can now be purchased. Algae that produce DHA are grown commercial-

make EPA or DHA but obtain it in 100 or 200 mg capsules under brand name Neuromins. the Nature's Way and Source Naturals market this product. This preparation, which is clearly superior to ALA, represents the best source of omega-3 fatty acids on the market.

> EPA and DHA, are both responsible for most of the health benefits of omega-3 fatty acids (See Table 1). If ALA is the only omega-3 you consume, then all of your EPA and DHA is made from this source. When you ingest ALA, some of it is converted to EPA and then DHA: this conversion is dependent on adequate amounts of vitamin B6. Under the best circumstances, this conversion is not very efficient in humans, and large amounts of ALA are needed to make barely adequate amounts of DHA. On the other hand, if you ingest just DHA, you will convert the DHA to EPA but not ALA. Ingesting DHA is a way of obtaining the health-promoting actions of EPA and DHA, without

the potential harm caused by ALA's ability to stimulate prostate cancer cell growth.

fetal development and in the neonatal period; and DHA deficiency can result in brain damage as well as impaired vision.

Later in life, dyslexia can be associated with impaired conversion of ALA to DHA. In a recent clinical trial, a significant number of children with dyslexia improved following DHA supplementation. There is a similar disorder, called dyspraxia, where movement, rather than reading, is impaired. This syndrome also improves with DHA supplementation. Depression in adults can be associated with low ly and the DHA extracted is sold DHA levels and successful treatment of this condition has been observed following supplementation with this lipid. In the literature, there is one reported case of schizophrenia associated with brain atrophy in which DHA supplementation reversed the brain atrophy, relieving the symptoms of this psychosis. Finally, there is some evidence that people on low fat diets who develop depression and other mental problems respond well to DHA administration.

A daily dose of 100-200 mg a day of DHA from algae is sufficient to maintain brain and heart function. The anti-inflammatory action of DHA requires a dose of at least 2 grams or more a day. The same appears to be true for the anticarcinogenic action of this fatty acid, as well as its impact on cancer-induced weight loss. The dose required to lower elevated blood pressure in men is less defined and may range from 100 mg to several grams a day. When would I use fish oil rather than

# **Table 1:OMEGA 3 FATTY ACIDS**

Prevent irregular heart beat Maintain normal brain function Support normal vision Lessen inflammation in rheumatoid arthritis, ulcerative colitis & asthma Reduce high blood pressure Block cancer cell growth & their ability to form new blood vessels Reduce weight loss caused by advanced cancer Lessen blood's ability to clot Lowers serum cholesterol levels

> Neuromins? In a patient with advanced prostate cancer and a projected survival of less than a year. Fish oil is a cheaper way of ingesting several grams of EPA and DHA, and the contaminants are not likely to become a problem.

> Are there any dangers in ingesting DHA? Well, the question becomes does DHA block the same pathways as does aspirin, indomethacin, and ibuprofen? A dose of several grams a

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day can increase the risk of gastric ulcer disease. After radiation therapy or surgery, recovery depends on the formation of new blood vessels. It is theoretically possible that an increase in DHA intake might slow or prevent full healing of normal tissue damage after these procedures.

The availability of Neuromins permits those on a vegan diet to obtain adequate, or even therapeutic, amounts of DHA and EPA without the dangers associated with ALA or fish oil.

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# **Quality Herbal Products**

One advantage of prescription drugs is that the quality and purity of the drugs are guaranteed by the FDA's supervision. As a result, one can depend on the fact that a medication I prescribe will have a standard amount of the drug in each capsule and will be free of contaminants. There is no similar program of supervision for herbal products. As a result, the quality of herbal products varies widely. While there are individual companies with high standards, it is difficult for a patient to find them.

Consumer Laboratories is beginning to fill this void (www.consumerlabs.com). They collect and test herbal products from a number of manufacturers and publish the names of those products that meet pre-established standards. We suggest that you inspect their recent review of saw palmetto extracts as an example. They have reviewed glucosamine, glucosamine/chondroitin sulfate, coenzyme Q-10, ginseng, and other products. You will find that certain manufacturers appear, time after time, as producers of quality products. You will also find some widely known vendors of herbal products conspicuous by their absence. We suggest you consult this site when deciding which product to buy.

# Saw Palmetto

Some of our readers take saw palmetto and speak of its virtues. We delayed making detailed comments on saw palmetto, because there was no evidence that this herb had any value in the management of prostate cancer. While saw palmetto extracts are reported to decrease the conversion of testosterone to dihydrotestosterone, none of the patients under our care experienced a decline in dihydrotestosterone levels while taking saw palmetto extracts. The reason for the discrepancy between the published literature and the experience of my patients has now been clarified -not all saw palmetto products contain an equal amount of the extract.

Saw palmetto is a compound derived from the fruit extract of the American Dwarf Palm Tree, which is native to the Atlantic Coastal Plain from North Carolina down through Northern Florida. The common herbal preparation represents the extracted lipids and sterols (chemicals with structural similarities to steroid hormones such as: testosterone and cortisone). There are many different ways to extract these lipids and sterols, yielding products with different biologic effects. Also, different brands and preparations vary in the amount of extract in each capsule.

Many people have asked me to recommend a particular manufacturer; until now I've hesitated, because there was no reliable information on the quality of the different brands. Now, Consumer Labs has tested 27 commercial products and found that only 17 contain an adequate amount of the specific fatty acids and sterols needed to produce a therapeutic effect. A list of the manufactures that passed this test is available at Consumer Labs' website.

A review of all clinical trials on saw palmetto in the treatment of BPH was reported in the Journal of the American Medical Association in 1998. After critically evaluating the quality of the clinical trials and the consistency of the results, the authors concluded that saw palmetto is an effective treatment for BPH. This conclusion has been confirmed in two subsequent extensive literature reviews (Wild and Boyle -- both published this year).

The FDA has approved Proscar as a treatment for BPH and male-pattern baldness. In the clinical trials comparing Proscar with saw palmetto, Proscar was found to be less successful than saw palmetto as a treatment for BPH.

Clinical trials are expensive but represent an additional means of determining the value of herbal products. The methods used to prepare specific herbal products vary between companies; the results of clinical trials on herbal products are therefore relevant only to the specific product tested. Most herbal product companies have been reluctant to participate in stringent and expensive tests of their products' value. Companies justified their position by claiming that consumers did not demand these studies and the cost of clinical trials eroded their profits. Fortunately, a few companies have taken part in clinical testing of their herbal extracts. In these situations, we have solid evidence of the value of an herbal product, as well as sound information about the effective dose and possible side effects. My policy is to name the herbal products that have been put through such testing; the companies that make the investment should be rewarded for their commitment to quality.

The saw palmetto product that has seen the widest clinical and laboratory testing is a European product called Permixon Complex (manufactured by CSG/Bio-Medic). You can order this product at www.800hairnow.com/hrlossprods.htm, where it is marketed as a product to reverse hair loss in men.

Why should this be listed as a product for treating baldness? For one thing, dihydrotestosterone plays a major role in the development of male-pattern baldness. Dihydrotestosterone is made from testosterone via the action of an enzyme called 5-alpha reductase. There are two forms of this enzyme, one is found in the prostate gland and the other in skin, including the scalp. Proscar is most active against the 5-alpha-reductase in prostate tissue but is less active against the enzyme found in the scalp. Permixon is reported to be active against both forms of this enzyme.

Permixon is a standardized preparation that has been well studied in the laboratory. In fact, most of the recent clinical studies on Saw Palmetto have been done using Permixon and I think it's value against BPH is now well documented.

The biochemical basis for the activity of Permixon against benign enlargement of the prostate almost certainly includes inhibition dihydrotestosterone formation within the prostate gland. Interestingly, Permixon inhibits formation of dihydrotestosterone in the prostate gland but not in many other tissues, and it does not alter blood levels of this hormone. However, this is not the whole story; Proscar is very effective in reducing prostatic dihydrotestosterone levels but is relatively ineffective in relieving the symptoms

of BPH. The action of testosterone and dihydrotestosterone on the prostate gland is markedly stimulated by the hormone prolactin. Permixon blocks the response of prostate cells to prolactin.

Permixon has been reported to inhibit the enzyme 5-lipoxygenase. The products of this enzyme play a very important role in prostate inflammation and edema formation. Dr. Jagat Ghosh, of my laboratory, has shown that the products of this enzyme promote the survival and growth of prostate cancer cells. The increased size of the gland in BPH can arise from an increase in the number of cells lining the prostate ducts, as well as an increase in the number of stromal cells in the space between the ducts. With this background, it is interesting to note that Permixon has been shown to cause the death of both the stromal cells and the cells lining the prostate ducts. This observation has been followed by a study showing that Permixon was able to slow the growth of prostate cancer cells and, at high enough concentrations, even kill these cancer cells. I can find no clinical trial testing Permixon in the treatment of prostate cancer, so it is difficult to know whether this observation is clinically relevant.

What do I recommend? This is a tough question. Consumer Labs doesn't list Permixon, but this could be because it was not tested or that it was tested and the retail version failed. At the moment, I am inclined to use Permixon, because of the published clinical and laboratory data. The effective dose appears to be two 160 mg capsules a day.

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# Patient Success Story

The most common reason men come to my second opinion clinic is for guidance in the management of newly developed hormone-resistant prostate cancer. Frequently, I find many patients do not have hormone-refractory prostate cancer and, with some adjustment, can be put back in remission or their disease can be held in check for prolonged periods of time. This month we will review an illustrative case.

W. S.'s story began when he developed repeated episodes of prostatitis, severe enough to cause the development of prostate stones. During our initial office visit, he gave me a bottle containing what must have been close to a hundred stones about 1/8th of an inch in diameter.

As is so often the case, the presence of prostatitis prevented the patient and his physicians from recognizing the development of prostate cancer until relatively late. At age 71 he went to a major teaching hospital on the East Coast for evaluation of his urinary tract problems. On June 10, 1997, W.S. was diagnosed with a Gleason grade 4+5 = 9 prostate cancer and a PSA of 5,000. CAT scans revealed cancer involving a large number of

lymph nodes in his pelvis, the back of his abdomen, and behind his clavicle on the left: The largest lymph node was approximately 2 by 4 inches. Additionally, he had a blood clot in the inferior vena cava, the major vein in the back of the abdomen that drains the pelvis and legs. A bone scan showed no clear evidence of bone involvement. His other medical problems included diabetes and heart disease.

Based on these findings his physicians diagnosed metastatic prostate cancer. They recommended surgical castration, which was done on June 18, 1997. By July 9 his PSA had declined to 1,300. By July 18 he was put on Casodex 50 mg. Thereafter, his PSA declined to a nadir of 70.7 ng/ml some six months after he was castrated. Unfortunately, by April 6, 1998 the PSA had increased to 96.9 ng/ml and he had to confront the threat of hormone-resistant prostate cancer.

I first saw W.S.in early July 1998 approximately one year after his initial diagnosis. At the time, his chief concern was that he might be developing hormone-refractory prostate cancer. At that visit, we made an interesting observation; his total testosterone was 33 ng/DL. After castration, the testosterone should be 20 ng/DL or below. Surgical castration can lead to a compensatory increase in androgen production by the adrenal glands, and I concluded that this was the most likely explanation for his modestly elevated testosterone level.

I was reluctant to leave him on his current treatment, because it was my judgment that this man had a very aggressive cancer that would quickly become uncontrollable. At this point, there were a number of other possibilities.

One option would have been to recommend ketoconazole followed by cytotoxic chemotherapy. His general medical status, which included diabetes and heart disease, made cytotoxic chemotherapy relatively unattractive. For example, the most effective chemotherapy combinations all use Emcyt, a drug that causes blood clots.

Another option would have been to place him on PC-SPES, but he already had a major blood clot that ruled this out.

The final option I considered was to intensify androgen withdrawal. This would involve increasing his Casodex dose from 50 to 100 mg and adding Proscar at a dose of 10 mg, which is what we ultimately chose. We also started him on Fosamax and Rocaltrol to reverse developing osteoporosis. As is usually my practice, we also recommended he start on Vitamin E 400 IU and Selenium-yeast 200 mcgs a day. Finally, we recommended that he adopt the low-fat diet detailed in our recent book Eating Your Way to Better Health.

On this program, his PSA gradually declined to 33.2 ng/ml within 14 months after we intensified his hormonal therapy. Unfortunately, his testosterone continued to increase to 53 ng/dL a day by 8/2/99. Two months later, his testosterone had increased to 65 ng/ml, and his PSA, 38.3 ng/ml, had now started to increase again.

Once more, the patient and I had to review his treatment options. It is important for you to understand that during the time he was on 100 mg Casodex and 10 mg Proscar, his quality of life was excellent and he wanted his condition to remain this way. One possible explanation for this clinical course was that his adrenal glands were compensating

by increasing their production of androgens.

Another remote possibility was that testicular tissue remained somewhere in his body and was gradually growing. Administration of Lupron or Zolodex has been reported to decrease adrenal androgen production by 30 to 50%. These drugs would be expected to suppress any testicular tissue, regardless of its location in the body. There is an additional reason why administration of an LHRH agonist, such as Lupron (leuprolide) might be beneficial. Human prostate cancer cells, even those known to be resistant to androgen withdrawal, possess LHRH receptors. When Lupron binds to these LHRH receptors, the growth of the cancer cells slows or stops altogether. He started on Lupron in early 2000. As of his last visit on 11/08/00, his PSA had declined from 38.3 to 7. 2 ng/ml and his testosterone level is now at castrate levels.

W.S.'s story illustrates a number of important points. Perhaps the most important is that some two and a half years after he was judged hormone-refractory at another institution, he is still responding to hormonal therapy. Secondly, it is a mistake to call someone hormonerefractory if they do not have caslevels of testosterone. trate Similarly, surgical castration does not guarantee castrate levels of testosterone; this needs to be confirmed by measuring the serum testosterone levels. I might add that considering his initial Gleason grade of 9 and PSA of 5,500 ng/ml, this man has done quite well.

### **Meatless Protein**

During the past several years, Rose and I have traveled throughout the United States, Europe, Australia, and the United Kingdom. As we discuss our dietary recommenda-

tions, we find that many patients are concerned that a diet without meat means a diet deficient in protein. We also found that most restaurants we dined in had no vegan or vegetarian options on the menu that contained an adequate amount of protein.

But it is actually quite easy to obtain adequate amounts of high quality protein on a diet that contains no meat, dairy products, or eggs. The key is a diet full of legumes, which are a rich source of protein. The protein in legumes combined with the protein in grains, produces a protein mix that often matches or exceeds the protein in meat. Most cuisines contain

# **Olive Oil Hummus**

# Shopping List:

- 1 cup dried chickpeas, boiled until soft
- 1/2 cup extra virgin olive oil
- 1 tablespoon roasted sesame oil
- I teaspoon salt (sea or kosher)
- 2 lemons or limes, juiced
- 1 garlic clove, minced
- Ground hot red chili pepper to taste
- 1/4 to 1/2 Madras curry (optional)

#### Preparation:

- Combine olive oil, cumin and garlic. Set aside.
- Puree water, lemon juice and chickpeas until smooth.
- Add the olive oil mixture, sesame seed oil and salt.
- Add red pepper and curry to taste.
- Serve with pita, toasted bread or crackers.

#### Prep Time:

15 minutes. Total time 1.5 hours.

#### Notes:

Serves 8-10. Each serving has approximately 10g of fat. There is only 1/2 teaspoon of sesame oil in each serving. In traditional hummus, sesame seed oil is used instead of olive oil.

legume-grain combinations that are quite tasty; some examples are: succotash (Native American), red beans and rice (Cajun), tofu and rice (Japanese), and pasta and beans (Italian).

Two other concerns keep people from using legumes: fear of gastrointestinal gas, and the time it takes to cook dried beans. It is easy to overcome these barriers.

First, legumes such as: peas, lima beans, lentils, and chickpeas (garbanzo beans) do not produce gas in most people.

Second, peas, lima beans, and lentils cook rapidly -- without the need for a prolonged period of soaking in water. I assume most of you have ready access to recipes for pea soup or succotash. Similarly, most of you have used frozen peas and lima beans. One of our favorite recipes is lentil and brown rice soup. You will find the recipe in our cookbook, as well as instructions on how to prepare grains and legumes.

# Hummus

We would like to introduce you to our variation of a traditional Mediterranean dish called Hummus, which features the legume known as the chick pea or garbanzo (Cicer arietinum). Hummus is traditionally made from pureed chickpeas, sesame seeds, garlic, lemon juice, and olive oil. It is used as a delicious spread on toast or crackers or when thinned, to make a salad dressing. Hummus keeps for quite a while in the refrigerator, so you can make a batch to use on sandwiches over the better part of a week.

But what is food without flavor, and in the grander sense we find that a bit of history only adds more spice to our dining experience. Apparently, archeologists have been investigating the origin of agriculture in the middle east and estimate that agriculture started

approximately 9,000 to 10.000 years ago in Iraq and Iran. What we find intriguing is that the founding crops included wheat, barley, and chickpeas all those years ago. So as you can see, the combination of grains and legumes is as much a part of our history as livestock and dairy products.

Sesame seeds are rich in oil and their addition makes traditional hummus high in fat. An additional problem is that sesame seed oil is rich in the fatty acid, linoleic acid. This fatty acid has been reported to stimulate the growth of prostate and breast cancers. On the other hand, it also contains a lignan, called sesamin that may have important anticarcinogenic activity. While we wait for further information on the safety of sesame seed oil, our daughter Gabrielle and I have created a version of hummus in which olive oil replaces most of the sesame seed oil. Our justification for this recipe is based on the recent report stating that the risk of prostate cancer declines as the intake of olive oil increases.

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# **Notes & Announcements**

Please **do not** send your medical information to Dr. Myers. He is unable to answer individual questions and **cannot** give advice on individual medical questions until that person is his patient.

We accept questions of a general nature (in writing) that Dr. Myers may address in a newsletter -- if he feels the information will be helpful to a number of subscribers.

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Mr. Keith Loring is on vacation this month.

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