Herbal update: 
Saw palmetto and the prostate

The burgeoning importance of alternative and complementary approaches to many common medical problems was highlighted by the publication in late 1998 of a group of special issues on alternative medicine by the American Medical Association. JAMA itself as well as various Archives journals featured articles on subjects such as traditional Chinese medicine for dermatologic disorders, herbal treatments in psychiatry, acupuncture for HIV-related peripheral neuropathy, and alternative medicine use among homeless youth.

The messages in these publications were mixed. In some studies little benefit was seen, while in others modest degrees of success were reported. Many investigators commented on the difficulties faced in evaluating data that derived from studies lacking rigorous statistical design. Others observed that short-term findings may not hold up with longer term follow-up. Nonetheless, these reports suggest that a sea change has occurred in the past few years, with clinicians across a wide range of specialties beginning to listen to their patients who have been clamoring for information on alternative medicine.

New thinking at the FDA
This change in attitude also can be seen in a recent distinct reversal of previous policy at the FDA. When the regulatory agency approved

Commentary
Timothy J. Wilk, MD, MPH

Timothy J. Wilk, MD, MPH, lead author of the systematic review discusses the implications of his study for primary care clinicians. Dr Wilk is Director, Department of Veterans Affairs Coordinating Center of the Cochrane Collaborative Review Group in Prostatic Diseases and Urologic Malignancies, Minneapolis Veterans Affairs Medical Center, Minneapolis, Minn.

"In our study, saw palmetto provided moderate improvement in urinary symptoms in men with mild to moderate symptoms of BPH. Readers should keep in mind, though, that although the usual dosage was 160 mg bid of S repens, the dosages of individual products on the market vary and the different formulations in these trials were neither standardized nor regulated. Also, the studies we analyzed were relatively short in duration, so it is not possible to determine whether saw palmetto has long-lasting benefits or reduces complications from BPH such as urinary retention or the need for surgery.

"The product appears to have few short-term side effects, but we could not comment on long-term safety because this was not addressed in the studies we reviewed. Randomized trials often either do not collect this information or have too few patients enrolled to detect potentially serious but uncommon events. Further research and clinical experience are needed, therefore, and men who are concerned about BPH should talk with their clinicians before taking any medication—herbal, over-the-counter, or prescription."
Guidelines for using saw palmetto

The Phytolinks' Desk refers to HerbalMedicines
specifically to the following guidelines for using saw palmetto
in men with benign prostatic hyperplasia.

**Indications and usage:** Prostate patients and imma-
table bladder in prostate hyperplasia stages I and II. The
medication relieves symptoms but does not reduce
pressure in the bladder.

**Precautions:** Patients with diabetes and liver or
prostate diseases should avoid using saw palmetto.

**Dosage:** 400 mg daily for 3-6 months.

finasteride for benign prostatic hyperplasia (BPH)
in the early 1990s, it also banned all nonprescrip-
tion remedies for the condition, claiming a lack of
evidence that any OTC agents were effective.1
FDA officials also expressed concern that the use
of OTC agents might result in patients failing to
seek medical attention should potentially serious
complications develop.

Today, in contrast, more than a dozen inde-
pendent new drug (IND) applications for alter-
native therapies are under review by the FDA,
including St John's wort for depression, Ginkgo
biloba for cognitive impairment, and saw pal-
metto for BPH. Less than a decade after being
banned as a therapeutic agent in the United
States, saw palmetto is now expected to be the
first herbal product to be licensed as a drug with
a specific indication.

**The herb and its history**

The saw palmetto (Serenoa repens) is a small,
scrubby palm tree found throughout the south-
eastern coastal United States. Some of these trees
are believed to be 500 to 700 years old. They
produce 3 to 7 new leaves each year; the individ-
ual leaves vary from 1.5 to 3 ft wide. During the
spring the plant produces clusters of white flow-
ers, and the bluish-black berries ripen throughout
the summer and into the fall. The fruit was used
by Native Americans in Florida in the early 1700s
as a food and to treat male genitourinary disor-
ders, and although saw palmetto fell out of favor
in this country during the 20th century, it
remained widely used for prostate problems in
Europe.

The hypothesized mechanisms of action of
S repens include inhibition of testosterone-5-alpha-
reductase, which converts testosterone to dihy-
drotestosterone, and alteration in steroid receptor
levels. Extracts of the fruit also exhibit antiedema-
tous and anti-inflammatory effects that may relate
to the inhibition of the cyclooxygenase pathway
and the arachidonic acid cascade.2

Continued
Reviewing the studies
A considerable body of clinical experience with phytotherapy for BPH has accrued in Europe, where in some countries plant-based remedies represent more than 90% of the treatments used for mild to moderate symptoms of the condition.8 A systematic review of the randomized, controlled trials of saw palmetto that have appeared in the worldwide literature since 1966 was included in the special alternative medicine issue of JAMA in November 1998.4 Of the 24 studies the investigators identified, 18 met the inclusion criteria for their analysis; 16 were double-blinded. A total of 2839 men were involved in these trials. Parameters measured were peak and mean urine flow rates and residual urine volumes.

Baseline symptom scores did not differ among the treatment groups surveyed, and comparisons were made of results with S repens alone versus results seen with finasteride and those seen with placebo. According to the investigators, "Results from participant and physician assessment indicated that S repens was superior to placebo and comparable with finasteride in improving urologic

Warning: The potential for cancer
That potential hazards exist in the use of alternative and complementary therapies, particularly when patients pursue these forms of treatment independently of medical advice, cannot be overemphasized. This point was made in a Wall Street Journal article.5 A North Carolina colleague whom I have known for many years wrote recently that 70% of his patients now regularly use herbal products and that the issue is on the minds of his patients. He told me that most patients do not discuss these products with their physicians for fear of being looked upon as "quacks" or "cranks," and that most patients do not look at the potential hazards involved. Moreover, his patients are so anxious to avoid the serious side effects of conventional medications for prostate disease that they will not ask about potential interactions with herbal products.5

"The number of men presenting with late-stage disease has declined tremendously during the past decade, and today only 25% to 30% of presenting cases are Stage D."

Of even greater concern is that some manufacturers are actively promoting their herbal products for use in preventing prostate cancer. One example is a product called PC-SPES, which is a combination of saw palmetto and several Chinese herbs. Because the marketing strategy is based on the manufacturers' statements that the name "SPES" derives from the Latin word for hope, the product is being targeted to men who may be at risk or desperate, and who are uninformed as to the potential hazards involved. There have been cases of cardiovascular complications and deep venous thrombosis with PC-SPES, yet it remains available without prescription in this country.

Physicians need to be better educated about alternative medicine. We in the United States are far behind our European colleagues in experience with botanical medicine. We need to incorporate this into our medical schools and combine the alternative approaches available to us with medical therapies as appropriate. If we are to do this, utmost importance will be physician-patient communication. Patients need to think of these products as "drugs," not harmless "immune boosters," and to understand that they should be taken only under medical supervision."
symptoms. A 28% improvement in urinary tract symptoms was seen among men taking S. repens, with a 25% improvement in nocturia, 24% improvement in peak urine flow, and 43% improvement in residual urine volume. Lower rates of erectile dysfunction were observed among those taking the herbal preparation. The investigators noted that a 3-month supply of saw palmetto typically costs between $10 and $50, compared to $200 for finasteride.

In conclusion, the authors stated, "The available evidence suggests that extracts from the saw palmetto plant, S. repens, improve urinary tract symptoms and flow measures in men with BPH. Compared with finasteride, S. repens produces similar improvements in urinary tract symptoms and flow measures, has fewer adverse treatment effects, and costs less." They do note, however, that it remains to be seen if the potential long-term complications of BPH are affected by saw palmetto treatment. Of particular concern is prostate cancer (see "Warning: The potential for cancer").


WRITTEN BY NANCY WALSH D'EPIRO

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Keeping safe with herbs: The 12 commandments

A new guide to help patients choose herbs that are safe for patients on medication or with medical conditions has been developed by Dr. Michael Ciriglione, MD, Assistant Professor of Medicine at the University of Pennsylvania School of Medicine, Philadelphia. "Clinicians are in an excellent position to offer advice and discuss risks and benefits pertaining to herbal treatments," Dr. Ciriglione observes. "To that end, clinicians should assume the responsibility of initiating a dialogue with their patients about any such products that patients may be using or may contemplate using." Further study regarding both safety and efficacy is clearly needed, he explains, for until more clinical experience with herbal treatments allows for more specific recommendations, these guidelines can help keep patients interested in alternative therapies safe.

1. All patients should be asked about use of herbal therapies and dietary supplements. Use of these agents should be documented in the medical record.

2. "Natural" does not necessarily mean safe.

3. Herbal-pharmaceutical interactions do occur; therefore, avoid combined use.

4. Lack of standardization of herbal agents may result in variability in herbal content and efficacy among manufacturers.

5. Lack of quality control and regulation may result in contamination during manufacture and potential misidentification of plant species.

6. Herbal treatments should not be used if the patient is contemplating pregnancy or during pregnancy or lactation because of lack of long-term clinical trials proving safety.

7. Herbal treatments should not be used in larger-than-recommended dosages.

8. Herbal treatments should not be used for more than several weeks because of lack of studies providing long-term safety.

9. Herbal treatments with known adverse effects and toxic effects should be avoided.

10. Infants, children, and the elderly should not use herbal treatments without professional advice.

11. An accurate diagnosis and discussion of proven treatment options are essential prior to the patient's considering use of herbal treatments.

12. Adverse effects should be documented in the patient's chart and therapy discontinued.

Adapted with permission from Ciriglione M, Sun A. Advising patients about herbal therapies [letter]. JAMA. 1998;280:1565-1566.