

# PHYTOTHERAPY IN CHRONIC PROSTATITIS

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## ABSTRACT

Chronic prostatitis is a very common condition that is poorly understood and has a significant impact on quality of life. Given the lack of proven efficacy of conventional therapies, such as antibiotics, it is not surprising that patients have turned with increasing frequency to phytotherapy and other alternative treatments. Although alternative therapies are plentiful, few have been subjected to scientific scrutiny and prospective controlled clinical trials. This review will cover phytotherapies commonly used in prostatitis patients and focus in detail on those with published data. These treatments include zinc, cernilton (bee pollen), quercetin, and saw palmetto. Although many of these therapies appear promising in small preliminary studies, phytotherapy requires the same scientific criteria for validation and acceptance as do conventional medical therapies. *UROLOGY* **60**: 35–37, 2002. © 2002, Elsevier Science Inc.

All prostatitis researchers can agree that patient and physician dissatisfaction over the management of this disease is high. It is not surprising, therefore, that patients often seek alternative forms of therapy. Phytotherapy, the use of plant-derived or “herbal” products, is gaining popularity in North America and is already the treatment of choice for many chronic conditions in Europe and Asia. Advantages of phytotherapy include (1) unique mechanisms of action, (2) typically low side-effect profiles, (3) low cost, and (4) a high level of acceptance by patients. A large disadvantage of phytotherapy in the United States is lack of US Food and Drug Administration (FDA) oversight, and indeed, consumer watchdog groups have found that many herbal preparations do not contain what is claimed on the label. Other disadvantages include (1) unknown drug interactions (sometimes leading to catastrophic results<sup>1</sup>), (2) no side-effect data collection, and (3) meaningless labels (to circumvent FDA regulations), such as “supports prostate health” or “promotes normal bladder function.”

Alternative herbal-based therapies are prevalent and popular in urologic disease in general and prostatic disorders in particular. Typical herbal therapies recommended for benign prostatic hypertrophy (BPH) with some clinical evidence of efficacy include saw palmetto (*Serenoa repens*),

stinging nettle (*Urtica dioica*), and *Pygeum africanum*.<sup>2</sup> Bee pollen extract (cernilton) has also been used with less evidence of efficacy for BPH.<sup>3</sup> Given the overlap of lower urinary tract symptoms between BPH and chronic prostatitis, these agents, either alone or in combination in “prostatic health” formulations, have also been recommended for men with prostatitis.

In patients with documented recurrent bacterial prostatic infection (category II), prolonged antibiotics remain the mainstay of therapy. Prolonged antibiotic use can alter intestinal flora, and use of probiotics (live beneficial bacteria) may reduce the incidence of gastrointestinal side effects.<sup>4</sup> Many men with category II prostatitis have recurrent urinary tract infections, and there is considerable interest in cranberry juice to treat cystitis in women, although randomized placebo-controlled data are lacking.<sup>5</sup> Cranberry juice may reduce *Escherichia coli* adherence and biofilm load in uroepithelial cells.<sup>6</sup> There are no published data on the efficacy of cranberry juice in prostatic infections, however, and it is possible that the acidity of the product could actually exacerbate symptoms. Zinc was one of the first factors with an antimicrobial effect to be identified in seminal plasma.<sup>7</sup> The initial discovery that many men with chronic bacterial prostatitis have low levels of zinc in the semen has led to the long-standing recommendation for zinc supplements in men with all forms of prostatitis. Unfortunately, oral intake of zinc does not appear to increase zinc levels in semen.<sup>8</sup> There are no published clinical trials that demonstrate the efficacy

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of zinc supplements for either treating or preventing prostatitis.

Category III (chronic pelvic pain syndrome [CPPS]) is the most common and enigmatic prostatitis syndrome. In the absence of infection, there is evidence for an inflammatory or autoimmune component to CPPS in some patients. Even in the absence of visible white blood cells, expressed prostatic secretions and semen of men with CPPS have elevated levels of inflammatory cytokines and oxidative stress.<sup>9–12</sup> Phytotherapy has been used most commonly in this category of prostatitis, and evidence for efficacy is actually more compelling than for other standard therapies.

Cernilton, an extract of bee pollen, has been used in prostatic conditions for its presumed anti-inflammatory and antiandrogenic effects. In a small open-label study, 13 of 15 patients reported symptomatic improvement.<sup>13</sup> In a larger more recent open-label study, 90 patients received 1 tablet of cernilton N 3 times daily for 6 months.<sup>14</sup> Patients with complicating factors (prostatic calculi, urethral stricture, bladder neck sclerosis) had minimal response, with only 1 of 18 showing improvement. In the “uncomplicated” patients, however, 36% were cured of their symptoms and 42% improved. Symptomatic improvement was typically associated with improved uroflow parameters, reduced inflammation, and a decrease in complement C3/coeruloplasmin in the ejaculate. Side effects in studies of cernilton for BPH and prostatitis have been negligible.

Quercetin is a polyphenolic bioflavonoid commonly found in red wine, green tea, and onions.<sup>15</sup> It has documented antioxidant and anti-inflammatory properties and inhibits inflammatory cytokines implicated in the pathogenesis of CPPS, such as interleukin-8.<sup>16</sup> In a preliminary small open-label study, quercetin at 500 mg 2 times daily gave significant symptomatic improvement to most patients, particularly those with negative expressed prostatic secretions cultures.<sup>17</sup> This was followed by a prospective, double-blind, placebo-controlled trial of quercetin 500 mg 2 times daily for 4 weeks using the National Institutes of Health Chronic Prostatitis Symptom Index (NIH-CPSI) as the primary endpoint.<sup>18</sup> Patients taking placebo had a mean improvement in NIH-CPSI from 20.2 to 18.8, and those taking quercetin had a mean improvement from 21.0 to 13.1 ( $P = 0.003$ ). In all, 20% of patients taking placebo and 67% of patients taking the bioflavonoid had an improvement in symptoms of  $\geq 25\%$ . A third group of patients received Prosta-Q (Farr Cabs, Santa Monica, CA), a commercial formulation containing quercetin with bromelain and papain, digestive enzymes known to increase the intestinal absorption of quercetin. In this group, 82% had a significant improvement in symptoms.

Saw palmetto is the most commonly used phytochemical for lower urinary tract symptoms and BPH, and indeed, some of the clinical studies with entry criteria based on symptoms likely included patients with CPPS. There have been no published studies of saw palmetto use in CPPS. A poster presented at the 2001 American Urological Association meeting compared therapy with saw palmetto or finasteride in CPPS patients for 1 year.<sup>19</sup> Although there was some improvement seen in the finasteride group, there was no improvement in the saw palmetto group.

Traditional Chinese medicinal therapies typically use acupuncture and herbal preparations. There are some publications with English abstracts that suggest significant improvement with this approach, although it is difficult to interpret formulation composition, entry criteria, and endpoint measures.<sup>20</sup>

In summary, phytotherapy shows much promise for prostatitis patients. In category II, probiotics can reduce the gastrointestinal side effects of prolonged antibiotic use. In category III, cernilton and quercetin have documented effects in both patient-reported improvement and improvement in biochemical markers of inflammation. Zinc, saw palmetto, and other agents used in BPH, such as stinging nettle and *Pygeum africanum*, do not have evidence for efficacy in CPPS. It is important that these phytotherapeutic approaches, and others, such as traditional Chinese medicine, be evaluated in prospective, randomized placebo-controlled trials with defined entry criteria and validated endpoints.

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## DISCUSSION FOLLOWING DR. SHOSKES' PRESENTATION

**Jackson E. Fowler, Jr., MD (Jackson, Mississippi):** It seems then that some of the best findings in terms of response and number of patients are found in the phytotherapy experience, which I know nothing about. It is surprising to me.

**Daniel A. Shoskes, MD (Weston, Florida):** You have to remember these were, in the aggregate, small studies of selected patients. However, in using these agents on a day-to-day basis in the clinic, I find there is a significant cohort who gets long-term complete relief. I think there are 2 patients enrolled in the Chronic Prostatitis Cohort Study<sup>1</sup> at the University of California Los Angeles whose symptom scores continue to be 0 or 1 and whose therapy was phytotherapy.

**J. Curtis Nickel, MD (Kingston, Ontario, Canada):** My personal impression is that a medical-oriented therapy is not going to be the answer, the cure-all to this condition. But when it

comes down to it, after antibiotics and  $\alpha$ -blockers fail, there are therapies that do work for the treatment-refractory patients. We looked at 100 patients who decided that they did not want to be involved in a placebo-controlled trial, and we observed them for a year using a standardized treatment algorithm. We have cured many of them, or "Mother Nature" has cured them. Something has cured them, because their symptom scores are 0 after 1 year of follow-up evaluation.

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