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## Herbal and complementary medicine in chronic prostatitis

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**Abstract** Chronic prostatitis is a very common and poorly understood condition with significant impact on quality of life. The etiology of prostatitis can be multifactorial and can present with a variety of symptoms. Given the lack of proven efficacy of conventional therapies such as antibiotics, many patients have turned to phytotherapy and other alternative treatments. This review will cover the alternative therapies commonly used in prostatitis with an emphasis on those with published data. These treatments include phytotherapy (quercetin, bee pollen) and physical therapy. Complementary therapies have shown the potential to help men with prostatitis, particularly when allopathic therapies have failed.

**Keywords** Prostatitis · Phytotherapy · Bioflavonoids · Complementary medicine

Prostatitis is one of the most prevalent conditions in urology. It is the most common urologic problem encountered in young men and accounts for a significant portion of men older than 50 years of age [10]. Unfortunately, the etiology, natural history and appropriate therapy for these patients is very unclear and poorly understood. While there is little controversy over the therapy for documented acute or chronic bacterial infections, the large majority of patients fall into the “non-bacterial” or “prostatodynia” group [chronic pelvic pain syndrome (CPPS), NIH prostatitis categories IIIa and IIIb]. Patient and physician dissatisfaction with these syndromes is high, making it an area ripe for patient

interest in non-traditional and alternative therapies. However, a major criticism of these alternative therapies is the common lack of properly designed scientific clinical trials. In fact, even those therapies considered as “standard” treatment for nonbacterial prostatitis have also not been evaluated in an accepted scientific fashion. For example, antibiotics are the most commonly prescribed therapy for nonbacterial prostatitis/prostatodynia, yet there is not a single prospective randomized placebo controlled trial documenting their effectiveness.

Alternative medical therapies and phytotherapy in particular are gaining popularity in North America. These treatments are often first line therapies for various chronic medical conditions in Europe and Asia. In the United States, Congress has taken such therapies out of the jurisdiction of the FDA as long as no claims for specific efficacy for medical illnesses are stated. This act of corporate largesse has several unintended but important consequences. First, there is no oversight of quality control on ingredients sold as herbal products. In fact, almost two thirds do not even have the ingredients stated on the label. Second, the manufacturers often provide meaningless descriptions such as “supports prostate health.” These advertisements force patients to search for products to treat their specific complaints without knowing if the product may have efficacy for BPH, prostatitis or prostate cancer. The advantages of phytotherapy include unique mechanisms of action, low side effect profiles, low cost and high patient acceptance.

In this review, we will discuss where phytotherapeutic agents and other alternative therapies may play a helpful role in the treatment of the various categories of prostatitis. While published literature is scarce, emphasis will be placed on therapies with some clinical evidence and scientific rationale for use.

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### Phytotherapy and prostatic disorders

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* [6]. Bee pollen extract (cernilton) has also been used with less evidence of efficacy for BPH. Lower urinary tract symptoms (LUTS) provide a complex but common connection between BPH and chronic prostatitis. Therefore, alternative agents, whether used alone or in combination for treatment of BPH, are also recommended for men with prostatitis.

Alternative and complementary therapies are also popular in men with prostate cancer. Since these agents either target prostate cancer cells or the side effects of therapy, they are seldom used in men with prostatitis.

Phytotherapy and other treatments which have been used or recommended for prostatitis are summarized in Tables 1 and 2.

### Category I prostatitis (acute bacterial)

The standard evaluation and therapy of category I prostatitis is straightforward and non-controversial. This is a serious bacterial infection with systemic cytokine release that can be fatal if not treated with appropriate antibiotics and supportive measures. Herbal or other alternative approaches to therapy, particularly those that prevent or delay conventional therapy, should be strongly discouraged.

### Category II prostatitis (chronic bacterial)

In patients with documented recurrent bacterial prostatic infection, the mainstay of therapy is long-term

antibiotics. Prolonged antibiotic use can create undue discomfort by altering intestinal flora. The use of probiotics, such as active culture yogurt, lactobacilli and other similar preparations, may reduce the incidence of gastrointestinal side effects. Many men with category II prostatitis also have recurrent UTI, and there is considerable interest in phytochemical therapy to prevent and treat cystitis. In current practice, cranberry juice has been used in women with cystitis. The theory is that cranberry juice may reduce *Escherichia coli* adherence and biofilm load in uroepithelial cells, however, there is a lack of randomized placebo controlled data. On a further note, there is no published data on the efficacy of cranberry juice in prostatic infections, and in fact it is possible that the acidity of the product could actually exacerbate symptoms.

Another well known supplement is zinc. It was one of the earliest factors identified in seminal plasma with an antimicrobial effect. The initial discovery that many men with chronic bacterial prostatitis have low levels of zinc in the semen has led to the longstanding recommendation for zinc supplements in men with all forms of prostatitis. Unfortunately, oral intake of zinc does not appear to raise zinc levels in semen. Furthermore, more recent studies question whether zinc levels are actually abnormal in prostatitis [20]. There are no published clinical trials that demonstrate the efficacy of zinc supplements for either treating or preventing prostatitis.

Prostatic drainage or "massage" was the mainstay of therapy for chronic prostatitis long before effective antimicrobials were available. In some patients whose prostates are congested with inflammatory debris, prostatic massage may drain obstructed areas not accessible to antibiotics. With the advent of antibiotics, prostatic massage has fallen out of favor to the point of being considered an "alternative" therapy by many

**Table 1** Phytotherapy

Phytotherapy	Common name	Mechanism	Use	Effect in prostatitis
<i>Serenoa repens</i>	Saw palmetto	?Anti-androgen	BPH	Minimal
<i>Urtica dioica</i>	Stinging nettle	?	BPH	Minimal
<i>Pygeum africanum</i>	N/A	?	BPH	Minimal
Cernilton	Bee pollen extract	Anti-inflammatory, anti-androgen	Prostatitis	42%
Quercetin	Prosta-Q	Anti-inflammatory, anti-oxidant	Prostatitis	67–82%

**Table 2** Alternative treatment of prostatitis

Treatment	Classification	Category of prostatitis	Mechanism
Yoghurt/lactobacilli	Supplement	Chronic bacterial	Reduce GI side effects
Cranberry juice	Supplement	Chronic bacterial	Reduce bacterial adherence
Zinc	Supplement	Chronic bacterial	Anti-microbial
Prostatic massage	Physical therapy	Chronic bacterial	Drainage
Biofeedback	Physical therapy	CPPS	Neuromuscular
Acupuncture	Physical therapy	CPPS	Neuromuscular
Cernilton	Phytotherapy	CPPS,ssymptomatic prostatitis	Anti-inflammatory, anti-androgen
Quercetin	Phytotherapy	CPPS	Anti-inflammatory, anti-oxidant, anti-fungal
Saw palmetto	Phytotherapy	CPPS	?Anti-androgen

urologists [11]. There is some evidence that at least a subset of patients who do not improve with antibiotics alone get durable sterilization of prostatic secretions and symptom relief with the combination of antibiotics and prostatic massage [17].

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### Category III prostatitis (chronic pelvic pain syndrome)

CPPS is by far the most common symptomatic prostatitis syndrome. The etiology and pathophysiology is controversial and in fact the disorder likely represents different underlying etiologies which produce a common symptom complex. In the absence of infection, there is evidence for an inflammatory or autoimmune component to CPPS. Even in the absence of visible WBC, EPS and semen of men with CPPS have elevated levels of inflammatory cytokines and oxidative stress [15]. Furthermore, the symptomatic response to antibiotics in CPPS patients may be due to direct anti-inflammatory effects of these drugs rather than their antimicrobial effects. Finally, much of the pain of CPPS is likely related to pelvic muscle spasm, which may be secondary to the infective or inflammatory conditions mentioned above, or may be the primary problem itself in the absence of any prostatic pathology.

CPPS can be divided into two categories, IIIa and IIIb, based on microscopic findings of WBCs. However, in terms of treatment, there is no evidence that patients in category IIIa have significantly different responses to therapy to those in category IIIb.

Typical therapies include antibiotics, alpha blockers, non-steroidal anti-inflammatories, muscle relaxants and thermal therapy. Scientific proof for the efficacy of these approaches is surprisingly weak. 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 anti-androgenic effects. In a small open label study, 13 of 15 patients reported symptomatic improvement [2]. In a larger more recent open label study, 90 patients received one tablet of Cernilton N tid for 6 months [13]. Patients with "complicating factors" (prostatic calculi, urethral stricture, bladder neck sclerosis) had minimal response with only one 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. It has documented anti-oxidant [12] and anti-inflammatory [5] properties and inhibits inflammatory cytokines implicated in the pathogenesis of CPPS such as IL-8 [14].

Finally, quercetin shows in vitro inhibition of androgen independent prostate cancer cell lines [9]. In a preliminary small open label study, quercetin at 500 mg bid gave significant symptomatic improvement to a majority of patients, particularly those with negative EPS cultures [18]. This was followed by a prospective, double blind, placebo controlled trial of quercetin 500 mg bid for 4 weeks using the NIH chronic prostatitis symptom index (NIH-CPSI) as the primary endpoint [19]. Patients taking placebo had a mean improvement in NIH-CPSI from 20.2 to 18.8 while those taking quercetin had a mean improvement from 21.0 to 13.1 ( $P=0.003$ ). Twenty percent of patients taking placebo and 67% of patients taking the bioflavonoid had an improvement of symptoms of at least 25%. A third group of patients received Prosta-Q (Farr Labs, El Segundo, Calif.), 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. Side effects are rare, although GI side effects can occur if taken on an empty stomach.

Several mechanisms may contribute to the beneficial effects of quercetin in CPPS. CPPS is associated with elevated oxidative stress in EPS and semen and patients who improve with quercetin have a reduction in oxidative stress metabolite F2-isoprostane in their EPS [6]. Furthermore, quercetin therapy reduces inflammation as measured by prostaglandin E2 levels in EPS and increases the levels of prostatic beta-endorphins [16]. Finally, quercetin does have weak antibacterial and antifungal properties which might conceivably play a role in CPPS [1].

Saw palmetto is the most commonly used phytochemical for LUTS and BPH, and indeed some of the clinical studies with entry criteria based on symptoms likely included patients with CPPS [4]. Although commercially promoted as "herbal Proscar", it is unclear whether the beneficial effects are from DHT blockade, alpha-1 receptor blockade or some other unknown mechanism. There have been no published studies of saw palmetto use in CPPS. In a presentation at the American Urological Association meeting in 2001, a study comparing saw palmetto with finasteride use for 6 months in men with CPPS found no improvement in the saw palmetto group.

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### Category IV prostatitis (asymptomatic)

There is no current evidence that asymptomatic inflammation in EPS, semen or prostate biopsy increases the risk for symptomatic prostatitis, BPH or prostate cancer. The primary harmful effects relate to an increase in prostate biopsies for non-malignant PSA elevation and potential impairment of sperm function. Since elevated oxidative stress is associated with category IV prostatitis, antioxidants such as those discussed for category III prostatitis may have the ability to treat category IV, if it indeed requires treatment.

## Other alternative therapies

An important concept regarding CPPS is the notion that there are specific anatomic areas that are centers for pain and discomfort. Specific causes may be linked to muscle spasms in the perineum or pelvic floor muscles, anatomic abnormalities such as hip arthritis, trauma, or previous surgery. CPPS may also be secondarily linked to voiding dysfunction, constipation, or unusual sexual activities. More difficult to evaluate are those associated with psychological issues such as anxiety or stress. Consequently there are numerous physical therapies to address these issues. Examples include yoga, heat therapy, neural modulation, acupuncture, and even self-hypnosis. Although interesting, these have yet to be tested using a standardized methodology.

Biofeedback requires CPPS to be resultant from muscle spasm or voiding dysfunction such as pseudo-dyssynergia. There have been limited studies showing some improvement in symptoms of CPPS [8]. However, more determinant studies are required to assess the particular group of individuals most likely to improve with biofeedback.

Traditional Chinese medicinal (TCM) therapies typically utilize acupuncture and herbal preparations. It is very difficult to interpret published studies of TCM in prostatitis because: (1) the English abstracts, when available, often use non-standard terminology, (2) it is often unclear which inclusion criteria are used, (3) outcome measures are not defined, (4) efficacy of acupuncture can be "operator dependent" and (5) the composition and purity of TCM herbal products in the USA share the same limitations as do other "Western" herbal preparations. Acupuncture has shown efficacy in some chronic pain syndromes and has been used in CPPS [3]. Several TCM herbal preparations with anti-inflammatory properties have been used, either orally or rectally, with claims for efficacy [7]. Hopefully, with the increasing interest in TCM in North America, some of these therapies will be tested in placebo controlled trials.

As can be imagined, there are many isolated claims worldwide of prostatitis cures using non-traditional therapies. Until sufficient information is published to allow analysis of data and duplication of results, not much can be made of these claims.

## Conclusions

Prostatitis and in particular CPPS can be frustrating for both patient and physician. For documented bacterial infections, antibiotics are still the therapy of choice, but probiotics are useful in ameliorating their side effects. In CPPS, there is credible clinical and scientific evidence that phytotherapy with cernilton or quercetin is safe, well tolerated and efficacious in the majority of patients. Other agents such as saw palmetto, *Pygeum*, and stinging nettle either have been shown to be ineffective in

CPPS or have not been studied in this patient population. Physical therapies such as acupuncture are a growing area in treatments but further standardized data must be collected. In general, there is an emergence of alternative therapies that are constantly forming. Most importantly, however, in order for any allopathic or alternative treatments to enter our therapeutic algorithms, they require evaluation in clinical trials with adequate controls, defined inclusion criteria and validated clinical endpoints.

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