The prostate is a walnut-sized gland that sits at the base of the male bladder, surrounding the prostatic urethra. As part of the reproductive system, this gland secretes seminal fluid, energizes sperm and provides for it a favorable alkaline medium. The prostate is subject to several disease states including infection, hypertrophy and cancer, causing pain, urinary frequency and urgency, inability to urinate, painful urination and sexual dysfunction.

Benign prostatic hyperplasia (BPH), prostate cancer, and prostatitis are its most common disorders. More than 50% of men in their sixties and as many as 90% of men in their seventies and eighties are diagnosed with BPH, resulting in 375,000 hospital stays each year in the United States alone. Prostate cancer is second only to cancer of the lung as the leading cause of cancer death among men. Each year, more than 100,000 new cases of prostate cancer occur in the US, and more than 30,000 deaths are caused annually by this disease. The good news is that over the past 20 years, the survival rate for prostate cancer has increased from 67% to 97%.

Unfortunately, benign prostatic hyperplasia (BPH) and prostate cancer do not have a known etiology, making prevention difficult and treatment less than ideal. Standard lines of treatment for these conditions, including pharmacological preparations, surgical and non-surgical procedures, hold significant risks. Additionally, as new theories about the functioning of the prostate gland develop, scientists are questioning the effectiveness and the rationale behind the continued use of these treatment modalities. A close review of the medical literature verifies the safety and efficacy of nutritional and botanical therapeutic agents such as Serenoa repens (saw palmetto), Urtica dioica (stinging nettle root), Prunus africcanum (pygeum), essential fatty acids, selenium, green tea extract, tomatoes and zinc to promote and maintain prostate health and alleviate urologic symptoms. In addition, select amino acids, in relatively physiologic doses, exhibit promising clinical results for the prostate patient. These natural ingredients effect a positive change in prostate health without the associated risk of adverse reactions. Following is a review of the most common prostate conditions and available treatment options, including a comprehensive evaluation of herbal and nutrient therapies for the prostate gland, scientific validity, positive patient outcomes, and incidences of negative side effects.

Benign Prostatic Hyperplasia (BPH; Prostate Enlargement; Lower Urinary Tract Symptoms (LUTS))

As a man ages, his prostate gland typically begins to enlarge. The medical community has no well-defined reason for this phenomenon, which is identified as benign prostatic hyperplasia (BPH), benign prostatic hypertrophy, or lower urinary tract symptoms (LUTS). This condition does not generally cause symptoms until a man reaches the age of 50, with the majority of associated problems peaking by age 70. BPH causes the prostate gland to constrict the urethra, making micturition increasingly difficult. As the bladder is forced to contract against increasing resistance, the bladder muscle (the detrusor) becomes hypertrophied and irritable. As the condition progresses, the bladder becomes unable to empty completely, and finally to empty at all. Residual urine in the bladder sets the stage for serious bladder infections and kidney malfunction.

Symptoms of BPH include:
- Reduced caliber and force of urine stream
- Frequent urination (particularly in the evening)
- Urinary urgency
- Leaking or dribbling
- Urinary retention (inability to pass urine)

Occasionally, a man may not realize that he has a urinary obstruction until he finds himself unable to urinate at all. Physicians refer to this type of episode as acute urinary retention, which can be triggered by a wide variety of drugs with anticholinergic side effects, both prescription and over-the-counter, such as anti-depressants, cold and allergy medications. These medications can tighten the bladder outlet, resulting in urinary retention. Alcohol, cold temperatures or a long period of immobility can also cause urinary retention when there is a partial obstruction present. Severe BPH can have serious long-term health effects such as urinary tract infections, bladder or kidney damage, bladder stones, painful intercourse, and incontinence.

Conventional Therapies for BPH

Finasteride (Proscar®), terazosin (Hytrin®), doxazosin (Cardura®, and tamsulosin (Flomac®) are medications approved by the FDA for the treatment of BPH. These pharmaceuticals aim at blocking DHT production or relaxing the prostatic urethra sphincter. Specifically, finasteride (Proscar®) inhibits the production of dihydrotestosterone (DHT), while terazosin (Hytrin®), doxazosin (Cardura®), and tamsulosin (Flomac®) force smooth muscle relaxation of the prostate and bladder neck. Nonsurgical treatments include transurethral microwave procedures (TUMT) and transurethral needle ablation (TUNA). Surgical treatments include open, laser and
transurethral (TURP) surgery. These treatments remove or destroy sections of the prostate gland. Botanical and nutritional therapies for BPH focus on decreasing the size of the prostate gland, preventing abnormal cell growth, and supplying the gland with nutrients to decrease the risk of infection, while maintaining hormonal balance and preserving the complete gland.

A Closer Look at Finasteride (Proscar)

Finasteride (Proscar®), a popular prescription for BPH, functions by interfering with the action of 5 α-reductase, the enzyme that converts testosterone into DHT in the prostate gland. DHT is an androgen that stimulates the synthesis of specific proteins and causes prostate cells to proliferate. The theory behind finasteride is that the body is producing too much testosterone and ultimately DHT, which is causing abnormal cell proliferation. By blocking the action of 5 α-reductase and ultimately DHT, which is causing abnormal cell proliferation. By blocking the action of 5 α-reductase and maintaining hormonal balance and preserving the complete gland.

Merck sponsored a double-blind placebo controlled study using finasteride (Proscar®) that demonstrated significant reductions in DHT, improvements in urinary function, and decreases in prostate volume in men with BPH. A bias may be present considering the sponsor of this research although there are more pressing issues regarding the use of finasteride. First, finasteride (Proscar®) only decreases the size of the prostate gland by 18% even though it reduces DHT levels by a surprising 80%. Further, only 37% of men using the drug for an entire year experience any symptom improvement. Sexual side effects of finasteride include decreased libido, impotence, and ejaculatory disorders. Finasteride (Proscar®) also increases a man's risk of developing prostate cancer. While this drug is in fact lowering DHT levels, it is clearly not promoting the health of the prostate gland. Moreover, the theory that DHT is the primary cause of abnormal cell growth is scientifically invalid, since a dramatic decrease in DHT levels plays a minimal role in preventing abnormal cell growth, and may even promote it. This theory represents a narrow and disconnected view of prostate function. A man's serum testosterone level falls as he ages. If testosterone causes BPH, then why would a man's risk of developing BPH increase as his levels of testosterone decrease? There is clearly more to this picture than that which medical scientists currently accept as fact.

The answer to this dilemma might be the growing imbalance between estrogen and testosterone levels in aging men. While estrogen levels remain relatively unchanged, testosterone or androgen levels fall dramatically as a man ages. However, in the stroma of the prostate (the area of tissue where BPH is thought to develop), DHT levels remain constant, while estrogen levels dramatically increase. The stroma produces additional estrogen (specifically estradiol) from testosterone in a process known as aromatization. Human sex hormone-binding globulin (SHBG) also affects the estrogen/testosterone ratio, since levels of SHBG increase with age. Normally, androgens like testosterone have an affinity for SHBG and cause cell proliferation. Medical researchers are discovering, however, that estrogen binds to SHBG as well, causing abnormal cell proliferation in the prostate. This information becomes particularly pertinent when viewed in light of the mechanisms of action of saw palmetto, nettle root and pygeum (discussed in detail in subsequent sections of this paper), and their clinical efficacy in the prevention and treatment of BPH and cancer.

Natural Therapies for Prostate

A Closer Look at Prostate Surgery

Most physicians recommend removal of the enlarged part of the prostate as the best long-term solution for patients with BPH. After any surgery for BPH, a Foley catheter is temporarily inserted through the penis to drain urine from the bladder into a collection bag while the surgical site is healing. This catheter frequently causes infection and recurring painful bladder spasms. Sexual function is affected in up to 30% of surgical cases, including retrograde ejaculation (which causes sterility). Furthermore, surgery for BPH does not prevent future prostate problems since a portion of the gland remains. Finally, scar tissue from the surgery typically forms in the urethra and causes narrowing (which is what the surgery is supposed to relieve). Patients with severe BPH who have already failed botanical and nutrient combinations and drug therapies may require surgical intervention to restore urinary flow. In order to prevent surgical intervention, it is essential to utilize noninvasive therapies at the onset of BPH symptoms or before. Medical professionals use pharmaceutical agents and surgical treatments as a standard approach to managing patients with moderate BPH. The risks of such therapies can outweigh their benefits. However, other scientifically valid therapies, including key nutrient and herbal combinations, are at least as effective clinically, without the associated risks.

Prostate Cancer

Cancer of the prostate gland is the most commonly diagnosed non-dermatological cancer among men. It is a leading cause of cancer death among American men, second only to lung cancer. In the United States, more than 30,000 men die each year from prostate cancer. One in five men will develop prostate cancer in his lifetime, and three percent of those will die from it.

The condition occurs when normal prostate cells turn cancerous (malignant) and divide at an unreasonable rate. It most often develops in the region of the prostate closest to the rectum. African-American men, men aged 65 and older, and men who have a first-degree relative with prostate cancer are at an increased risk. Black Americans have the highest incidence in the world. Interestingly, there is a direct correlation between intake of animal fat and the risk of getting prostate cancer. The National Cancer Institute established that total consumption of animal fat directly relates to the risk of advanced prostate cancer. Red meat has the strongest positive association with advanced prostate cancer.

Symptoms

There are essentially no warning signs for early prostate cancer. As the cancer advances, some men may experience symptoms similar to those associated with BPH (urinary frequency, urgency, pain with urination, etc.) or a urinary tract infection.

Early Detection and Treatment

There is no scientific evidence that provides a definite link between early detection and even treatment of prostate cancer and the incidence of deaths caused by this disease.
Natural Therapies for Prostate

a health professional diagnoses a man with early stage prostate cancer, it is highly likely that he will then be required to undergo invasive evaluation. If this evaluation results in cancer detection, then standard treatments are generally employed. Standard treatments such as surgery, radiation therapy, hormonal therapy and occasionally chemotherapy have serious side effects including incontinence (lack of bladder control), impotence (inability to have an erection), and even death. One treatment option for men with early-stage prostate cancer is "watchful waiting." Since many prostate cancers are small and very slow-growing, physicians may opt to shun treatment altogether (watchful waiting), which is an accepted approach to managing the condition. A benefit of this method is that it avoids any potential side effects that may occur with other forms of treatment. Men choosing this method of treatment (or lack thereof) often turn to nutrient and botanical therapies as a means of safely treating their cancer. Interestingly, a study completed at the University of Pennsylvania Hospital found that one third of all prostate cancer patients supplement medical treatment with complementary therapies.

Prostatitis

Acute bacterial prostatitis is an acute infection of the prostate gland. Bacteria usually migrate to the prostate from the urinary system. As the infection advances, the gland begins to swell, causing sudden symptoms of painful, urgent, and frequent urination. Other symptoms include fever and chills, and pain over the bladder, lower back and between the testicles and rectum (the perineal area). The standard medical treatment for acute prostatitis is usually intravenous antibiotics until the fever breaks, followed by 4-6 weeks (or longer) of oral antibiotic therapy. It is critical that one seeks medical attention promptly if he experiences fever-associated pain in the areas described above.

Chronic bacterial prostatitis is usually symptomatic, causing vague, persistent, low back and perineal pain, urinary urgency and frequency, and painful urination. Standard medical treatment is oral antibiotic therapy for 2 to 3 months. Patients can also experience prostatitis that is not the result of a bacterial invasion. This condition is referred to as chronic non-bacterial or non-infectious prostatitis. Chronic non-bacterial prostatitis is more common than bacterial prostatitis, and has the same symptom picture. Having no known cause, healthcare professionals find it difficult to treat. It does not respond to antimicrobial agents. Serenoa repens (saw palmetto), Urtica dioica (stinging nettle root), Prunus africanum (pygeum), zinc, selenium, green tea extract, tomatoes, amino acid therapy, and essential fatty acid therapy are effective and safe treatment options for nonbacterial, non-infectious prostatitis.

Botanical and Nutritional Therapeutic Options for Prostate Conditions

**Serenoa repens (Saw Palmetto)**

**Description and Medical History:** Saw palmetto is native to North America. It is a member of the palm family and has characteristic sharp edges that can literally "saw" through clothing, hence its common name, saw-palmetto. The plant produces a one-seeded dark brown-to-black berry that is harvested and used in the preparation of phytomedicines. Researchers now focus on the lipophilic medicinal extracts of these berries, although one should not ignore its historic use as a whole berry preparation. Traditionally used for the treatment of prostate conditions, saw palmetto was appropriately referred to as the "old man's friend." Touted for its effectiveness in reducing prostate inflammation, alleviating chronic urinary tract infections, and increasing sperm count, this herb has demonstrated the added benefit of increasing sex drive in men.

**Known Medicinal Constituents**

- Lipid constituents: Phytosterols, particularly beta-sitosterol, tri, di, and monoglycerides, and free fatty acids
- Flavanoids and polysaccharides

**Indications for Use (specific to prostate health)**

- Mild to moderate benign prostatic hyperplasia
- Non-infectious (non-bacterial) prostatitis
- Prostate cancer

**Possible Mechanisms of Action**

- Has alpha-adrenoreceptor and calcium blocking activities (antagonists) that function to relieve urinary urgency by reducing the smooth muscle contractions of the bladder sphincter

**Table 1.1 Double Blind Placebo-Controlled Clinical Trials of Saw palmetto Extract in BPH Patients**

<table>
<thead>
<tr>
<th>Researchers</th>
<th>Daily Dosage (mg/b.i.d.)</th>
<th>Regime</th>
<th># of Patients Saw palmetto group (SP) vs. Placebo</th>
<th>% Reduction in Urinary Frequency (at night)</th>
<th>% Increase in Peak Urinary Flow Rate</th>
<th>Tolerability of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tasca et al. (1985)</td>
<td>160 x 1-3 mo</td>
<td>SP: 14</td>
<td>Placebo: 13</td>
<td>SP: 74% Placebo: 39%</td>
<td>SP: 26% Placebo: 5%</td>
<td>Excellent</td>
</tr>
<tr>
<td>Reece Smith et al. (1986)</td>
<td>160 x 3 mo</td>
<td>SP: 33</td>
<td>Placebo: 37</td>
<td>SP: 36% Placebo: 36%</td>
<td>SP: 35% Placebo: 35%</td>
<td>Excellent</td>
</tr>
<tr>
<td>Emili et al. (1983)</td>
<td>Unclear x 1 mo</td>
<td>SP: 15</td>
<td>Placebo: 15</td>
<td>SP: 50% Placebo: 13%</td>
<td>SP: 33% Placebo: 2%</td>
<td>Excellent</td>
</tr>
<tr>
<td>Descotes et al. (1995)</td>
<td>160 x 1 mo</td>
<td>SP: 62</td>
<td>Placebo: 94</td>
<td>SP: 33% P&lt;0.05 Placebo: 18%</td>
<td>SP: 29% P&lt;0.05 Placebo: 9%</td>
<td>Good</td>
</tr>
<tr>
<td>Cukier et al. (1985)</td>
<td>160 x 2-3 mo</td>
<td>SP &amp; Placebo: 146</td>
<td></td>
<td>SP: 33% P&lt;0.001 Placebo: 15%</td>
<td>N/A Placebo: N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Champault et al. (1984)</td>
<td>160 x 1 mo</td>
<td>SP: 47</td>
<td>Placebo: 41</td>
<td>SP: 46% P&lt;0.001 Placebo: 15%</td>
<td>SP: 50% P&lt;0.001 Placebo: 5%</td>
<td>Excellent</td>
</tr>
<tr>
<td>Boccafoshchi &amp; Annoscia (1983)</td>
<td>160 x 2 mo</td>
<td>SP: 11</td>
<td>Placebo: 11</td>
<td>SP: 55% P&lt;0.05 Placebo: 32%</td>
<td>SP: 43% P&lt;0.05 Placebo: 19%</td>
<td>Excellent</td>
</tr>
</tbody>
</table>

*P<0.001 - < 0.05 vs. placebo*
• Exhibits mild 5-alpha reductase inhibition activity in the prostate gland 25,26.
• Inhibits the arachidonic acid cascade via the inhibition of cyclooxygenase and 5-lipoxygenase in the prostate 27.

**Double-Blind Clinical Trials with Saw Palmetto in BPH**

Wilt et al. 28 conducted a systematic review and quantitative meta-analysis of the existing evidence regarding the therapeutic efficacy and safety of saw palmetto plant extracts in men with mild to moderate benign prostatic hyperplasia (BPH). The researchers evaluated 18 randomized controlled trials that included 2,939 men with a mean age of 65 years. Sixteen of these studies (89%) were double-blinded and placebo controlled, and the mean duration of the studies was 63 days. The researchers measured the efficacy of saw palmetto extracts in affecting urologic symptoms, urine flow, residual urine volume, prostate size and nocturia. The study participants (that were treated with saw palmetto) and their physicians reported significant improvements in BPH symptoms compared to the placebo group. The men had decreased urinary tract symptom scores overall, fewer episodes of nocturia (-0.76 times per night), and an increase of peak urine flow rates (1.93 mL/s [95% CI, 0.72-3.14]). All trials in this meta-analysis produced similar improvement in urinary tract symptoms and urinary flow rates when measured against finasteride, and were associated with significantly fewer adverse side effects. Table 1.1 highlights seven key placebo-controlled clinical trials with a liposferolic extract of saw palmetto, all of which were a part of the recent systematic review by Wilt et al. 29 In six out of seven of the studies, urinary frequency was dramatically decreased in the saw palmetto treatment group as compared to the placebo group. The saw palmetto group experienced a significant improvement in peak flow rates (26-50%) compared to the placebo group (2-35%). While symptom score evaluations are a valuable means of analyzing outcomes, the researchers did not routinely complete these evaluations since many of the studies were done before this methodology was widely accepted. 30

**Finasteride vs. Saw Palmetto Extract**

Carraro et al. 30 completed the largest international comparative trial for the treatment of BPH. This double-blind study compared the therapeutic effects of finasteride versus saw palmetto extract in 1,098 patients with moderate BPH. The most critical observation of this comparative trial was that saw palmetto extract does not have a significant effect on serum PSA levels or prostate volume. With this knowledge, physicians do not need to be concerned that saw palmetto will affect PSA levels and mask prostate cancer. **This clinical evidence also makes it clear that the primary action of saw palmetto is not its ability to inhibit 5-alpha reductase, since PSA levels remained relatively constant.** Table 1.2 further highlights the results of this study.

### Table 1.2 Double-Blind Trial Comparing the Therapeutic Effects of Saw Palmetto Extract with Finasteride in Patients with Moderate BPH 30

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Saw Palmetto Extract</th>
<th>Finasteride</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Dosage</td>
<td>320 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>Quality of Life</td>
<td>36% improvement</td>
<td>41% improvement</td>
</tr>
<tr>
<td>Peak Flow Rate</td>
<td>25%</td>
<td>30% p&lt;0.05</td>
</tr>
<tr>
<td>Prostate Volume</td>
<td>-6%</td>
<td>-18% p&lt;0.001</td>
</tr>
<tr>
<td>PSA</td>
<td>No change</td>
<td>-41% p&lt;0.001</td>
</tr>
<tr>
<td>IPSS</td>
<td>-37%</td>
<td>-39%</td>
</tr>
</tbody>
</table>

*Patients reported more sexual dysfunction with finasteride and reported a significantly higher number of incidences of impotence and decreased libido p<0.001 on sexual function score

IPSS= international Prostate Symptom Score  PSA= prostate-specific antigen

**Natural Therapies for Prostate**

**Overview: Clinical Effects of Saw Palmetto (Serenoa repens)**

- Decreases urinary urgency
- Decreases perineal pain
- Decreases nocturnal (nighttime) frequency
- Increases urinary flow rate
- Prevents infections due to residual urine
- Reduces residual urine
- Improves quality of life for BPH patients

**Contraindications**

Pregnancy and lactation: it is possible that Saw palmetto may be unsafe for pregnant and lactating women due to its antiandrogen and estrogenic activity. 31

**Side Effects**

Tolerability is generally excellent for Saw palmetto although it can in rare instances cause headache or mild gastrointestinal disturbances. 32

**Possible Interactions with Drugs**

May interfere with oral contraceptives and hormone therapy due to its antiestrogen effect. 33

**Possible Interactions with Herbs and other Dietary Supplements**

None known

**Possible Interactions with Lab Tests**

None: Saw palmetto does not have a significant effect on serum PSA levels. 34

**Recommended Dosage**

Lipophilic Extract: 160 mg b.i.d., according to research studies referenced in this review (may be reduced if combining with dried berries)

Dried berry: .5-1 gram t.i.d.

**Urtica dioica (Stinging Nettle Root)**

**Description and Medical History:** Nettle is a weed that has a particular affinity for nitrate-rich soil, found in most temperate regions of the world. Its root and rhizome (the parts used today for the treatment of prostate conditions) are long and yellow-brown in color. According to the Eclectics, nettle root (including the rhizome) relieved bronchial and asthmatic trouble. Healers also used nettle as a diuretic and astringent, and as a treatment for joint ailments. 35 Its high lignan content made it an attractive fiber source before the introduction of flax seeds. As mentioned earlier in this review, estrogen and androgens such as testosterone bind to SHBG and cause cell proliferation. As a man ages, his SHBG levels increase, making him more susceptible to abnormal cell proliferation. Today, researchers are finding the high lignan content of nettle to be responsible for the root's ability to bind to SHBG (sex hormone binding globulin), a key to its potential use as a prostate cancer remedy. 36,37 This strong affinity for SHBG limits the amount of testosterone and estrogen that can bind to it and influence cell proliferation.
Natural Therapies for Prostate

> **Known Medicinal Constituents**

- Scopoletin (a coumarin)
- Lignans (Urtica dioica agglutinin [UDA], (-)-secoisolariciresinol)
- Sterols and steryl glycosides (including sitosterols)

**Indications for Use (specific to prostate health)**

- Mild to moderate benign prostatic hyperplasia\(^{34,35}\)
- Non-infectious (non-bacterial) prostatitis\(^{34,36,37}\)
- Prostate cancer\(^{33}\)

**Possible Mechanisms of Action**

- Inhibition of sodium-potassium ATPase from BPH tissue, thereby decreasing androgen response\(^4\)
- Reduction of human sex hormone-binding globulin (SHBG) activity due to lignans found in nettle root\(^\text{34,38}\)
- Antagonism of the pathway by which SHBG leads to the induction of androgen-responsive genes\(^39\)
- Inhibition of human leukocyte elastase (HLE), a marker in prostatitis and associated lower urinary tract infections (LUTI)\(^37\)
- Weak inhibition of DHT binding to cytosolic androgen receptors in the prostate\(^39\)
- Inhibition of aromatase, thereby inhibiting the conversion of androgens to estrogens\(^38\)

**Placebo Controlled Clinical Trials Involving Stinging Nettle Root in BPH patients**

The popular use of stinging nettle root extract in Germany encouraged the onset of numerous clinical trials. Collectively, these trials demonstrated the benefits of using nettle root for the treatment of BPH. In a 1996 placebo controlled trial, Engelmann et al.\(^40\) successfully demonstrated that nettle root extract was superior to placebo in terms of the International Prostate Symptom Score (IPSS). The study included 41 subjects with mild BPH, observed for a period of 3 months. In another placebo controlled trial (1987), 79 patients with BPH were given either nettle root extract or placebo for as long as two months. The dosage was 600 mg per day for the duration of the study. Nettle root proved to be better than the placebo in all parameters that were measured including urinary flow, residual urine and urinary volume. In 1985, Vontobel et al.\(^42\) conducted a placebo controlled clinical trial that demonstrated a significant improvement in urinary flow and micturition volume, and an impressive decrease in SHBG \((p<0.0005)\). The study included 50 patients that were prescribed 600 mg of nettle root extract daily for approximately two months.

**Placebo Controlled Clinical Trials of Stinging Nettle Root/ Saw Palmetto Combination Therapies**

Metzker et al.\(^43\) completed a double blind placebo controlled clinical trial involving 40 BPH patients that took either a placebo treatment or a mixture of nettle root and Saw palmetto extracts for 6 months. The experimental group showed a dramatic improvement in IPSS (International Prostate Symptom Score) as compared to the placebo group. Additionally, urinary flow rates improved significantly in the experimental group compared to the placebo group. Details of this study are highlighted in Table 2.1. The 6-month double blind treatment was followed by an open-label extension. Interestingly, the placebo group demonstrated a marked improvement in urinary flow rates from 15.50 to 17.5 ml/sec. However, the group receiving the saw palmetto/nettle extract demonstrated a further statistically significant increase in urinary flow rate with continued therapy for one year.

<table>
<thead>
<tr>
<th>Table 2.1</th>
<th>320mg Saw Palmetto Extract + 240 mg Nettle Root Extract for 6 months</th>
<th>Placebo for 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPSS</td>
<td>18.3 - 11.1</td>
<td>19.0 - 17.06</td>
</tr>
<tr>
<td>(40% decrease in symptoms)</td>
<td>p&lt;0.05</td>
<td>(7% decrease in symptoms)</td>
</tr>
<tr>
<td>Urinary Flow Rates</td>
<td>Improved from 14.65 - 17.95 ml/sec (23% improvement)</td>
<td>Improved from 15.05 - 15.50 ml/sec (4% improvement)</td>
</tr>
</tbody>
</table>

**IPSS = International Prostate Symptom Score**

Sokeland et al.\(^44\) completed another comparison trial with finasteride and a saw palmetto/nettle root extract.

<table>
<thead>
<tr>
<th>Table 2.2</th>
<th>Daily Dosage Duration</th>
<th>IPSS (International Prostate Symptom Score) % Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finasteride Group</td>
<td>5 mg 12 months</td>
<td>47% improvement -5.6 point change</td>
</tr>
<tr>
<td>Saw Palmetto/ Nettle Root Group</td>
<td>160 mg saw palmetto liposterolic extract/120 mg nettle root extract b.i.d 12 months</td>
<td>42% improvement -4.8 point change</td>
</tr>
</tbody>
</table>

This randomized, double-blind, multicenter clinical trial involved 543 patients suffering from BPH stages I and II. Both therapies proved to be similar in effectiveness in all areas including: IPSS scores, urination times, and urinary flow rate. The major difference was in tolerability. Patients tolerated herbal therapy better than finasteride. The finasteride group reported more adverse events including diminished ejaculation volume, erectile dysfunction and headaches. Table 2.2 highlights dosages, duration and IPSS scores for this study.

**Overview: Clinical Effects of Stinging Nettle Root (Urtica dioica)**

- Decreases urinary urgency
- Decreases nocturnal (nighttime) frequency
- Encourages hormonal balance
- Increases urinary flow rate
- Prevents infections due to residual urine
- Reduces residual urine
- Reduces risk of abnormal prostate cell proliferation
- Improves quality of life for BPH patients

**Contraindications and Warnings**

Pregnancy and lactation: insufficient reliable information. Avoid using unless under the strict supervision of a qualified healthcare practitioner. Benign prostatic hyperplasia (BPH) therapies and prostate cancer therapies should be monitored by a qualified healthcare practitioner.

**Side Effects**

Tolerability is generally excellent for nettle root.\(^45\)

**Possible Interactions with Drugs:** None known

**Possible Interactions with Herbs and other Dietary Supplements:** None known

**Possible Interactions with Lab Tests:** None known
**Pygeum africanum** (Pygeum)

**Description and Medical History:** Pygeum, sometimes referred to as African Plum Tree, is a large evergreen tree that grows in the higher plateaus of southern Africa. The Eclectics and other healers traditionally collected the bark of the tree, ground it into a powder, and prescribed it as a tea for genito-urinary conditions. It was also used as an aphrodisiac, and as a remedy for "madness." Medical researchers now consider pygeum bark to be a scientifically valid and clinically effective remedy for functional symptoms of benign prostatic hyperplasia (BPH) that include nocturia, dysuria, micturitional disorders, and bladder fullness.

**Known Medicinal Constituents**
- Phytosterols (including beta-sitosterol, beta-sitosterone and campesterol)
- Ferulic esters of long chain fatty acids
- Pentacyclic triterpenes (including oleanolic, crataegolic and ursolic acid)

**Indications for Use (specific to prostate health)**
- Mild to moderate benign prostatic hyperplasia
- Non-infectious (non-bacterial) prostatitis
- Prostate cancer
- Decreases urinary urgency
- Decreases nocturnal frequency

**Possible Mechanisms of Action**
- Beta-sitosterols found in Pygeum inhibit prostat gland synthesis, thereby reducing the abnormal high levels of prostaglandins normally found in BPH patients.
- Pygeum prevents bladder contractile dysfunction, thereby reducing risk of prostatitis and/or BPH complications.
- Pygeum is a potent inhibitor of prostatic fibroblast proliferation via its ability to inhibit protein kinase C activation. Rapidly growing benign and malignant cells require protein kinase C activity.
- Pygeum antagonizes 5-lipoxygenase metabolite production, thereby decreasing bladder hyperreactivity and prostate inflammation.
- Ferulic acid esters reduce prostatic cholesterol levels, thereby limiting synthesis of testosterone.
- Triterpenes, including oleanolic, crataegolic and ursolic acid decrease inflammation in prostate tissue.
- Pygeum competes with androgen precursors.

**Placebo-Controlled Clinical Trials Involving Pygeum Bark and BPH patients**

Pygeum bark extract is a popular treatment in Europe, particularly in central and Eastern Europe. Breza et al. conducted a multicenter trial in central Europe in 1998 to determine the efficacy and safety of using Pygeum africanum extract in the treatment of BPH. The researchers evenly distributed 85 patients with mild to moderate BPH among three centers. IPSS scores decreased by 40% and quality of life scores by 32%. There was also a statistically significant reduction in nocturnal frequency (32%) although urinary flow parameters remained unchanged. The researchers reported a particularly satisfactory safety profile. An interesting aspect of this study was the researchers' decision to follow the patients after the initial treatment for an additional month with no treatment. The results of the treatment remained positive even after it was stopped, indicating a persistent therapeutic activity. Table 3.1 highlights the results of this study.

<table>
<thead>
<tr>
<th>Table 3.1</th>
<th>Pygeum africanum Extract Administered as 50 mg bid and 100 mg qd</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPSS (2 month comparative phase)</td>
<td>36% mean improvement</td>
</tr>
<tr>
<td>QOL (2 month comparative phase)</td>
<td>28% mean improvement</td>
</tr>
<tr>
<td>Qmax (2 month comparative phase)</td>
<td>16% increase</td>
</tr>
<tr>
<td>Tolerability (2 month comparative phase)</td>
<td>Excellent</td>
</tr>
</tbody>
</table>

**Overview:** These clinical trials coupled with the results of earlier in vitro trials clearly show that Pygeum africanum bark extract:
- Decreases nocturnal frequency
- Decreases urinary urgency
- Improves quality of life for BPH patients
- Inhibits prostate cell proliferation
- Reduces prostate size
- Reduces residual urine
- Does not affect serum hormone levels
- Is very well tolerated
Natural Therapies for Prostate

Contraindications
Pregnancy and lactation: insufficient reliable information. Avoid using unless under the strict supervision of a qualified healthcare practitioner.

Side Effects
Tolerability is generally excellent for Pygeum africanum bark, although some researchers speculate that it may, in rare instances, cause nausea and mild abdominal pain. Avoid using unless under the strict supervision of a qualified healthcare practitioner.

Possible Interactions with Drugs: None known
Possible Interactions with Herbs and other Dietary Supplements: None known

Recommended Dosage: 100-200 mg lipophitic extract (12-14%) per day in 6-8 week cycles, according to research studies referenced in this review.

*It is advisable to be mindful of the source for pygeum used since over harvesting may be threatening the species.*

Green Tea
The Prostate Cancer Research Institute reports on its web page that green tea and a lipid-extract from it contain several pharmacologically active chemicals in the flavonol group of polyphenols known as catechins. In addition to being anti-oxidants and free-radical scavengers, these compounds inhibit the expression of oncogene and the action of three enzymes believed to play a role in oncogenesis. They have demonstrated anti-cancer activity in laboratory mice carrying human prostate and breast cancers and mouse lung and skin cancers.

Two catechins found in green tea, epicatechin gallate (ECG), and epigallocatechin-3 gallate (EGCG) are inhibitors of 5-alpha reductase which may be effective in the treatment of 5 alpha dihydropistosterone-dependent abnormalities, such as benign prostate hyperplasia and prostate cancer. It may be possible that these catechins are regulating androgen action in the prostate gland. As described earlier in this article, 5 alpha-reductase is the enzyme that converts testosterone into DHT in the prostate gland. DHT is an androgen that stimulates the synthesis of specific proteins and causes prostate cells to proliferate. The theory behind 5-alpha reductase blocking agents is that the body is producing too much testosterone and ultimately causing abnormal cell proliferation. By blocking the action of 5 alpha-reductase, the prostate gland should shrink.

Alanine, Glutamine, and Glycine
In 1958, Feinblatt and Gant completed a controlled crossover study using a combination of alanine, glutamine and glycine to treat BPH symptoms. The study included 40 men with confirmed BPH. After 3 months on the amino acid combination, the authors reported that delayed micturition was either relieved or reduced by 70%, nighttime urinary frequency was reduced by 95%, and urinary urgency decreased by 81% and urinary frequency decreased by 73%. These preliminary results inspired the work of Damrau in 1962. He conducted a controlled study that included 45 cases of uncomplicated BPH in an experimental group and 40 cases of uncomplicated BPH in a control group. The age, weight and height of all subjects were closely matched. The experimental group received the combination amino acid therapy daily for three months. Table 4.1 reveals the results of this study.

<table>
<thead>
<tr>
<th>Table 4.1 Amino Acid Therapy for BPH (Modified from Damrau P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
</tr>
<tr>
<td>----------</td>
</tr>
<tr>
<td>Nocturia</td>
</tr>
<tr>
<td>Urgency</td>
</tr>
<tr>
<td>Frequency</td>
</tr>
<tr>
<td>Delay in starting</td>
</tr>
<tr>
<td>Difficulty maintaining urination</td>
</tr>
</tbody>
</table>

Damrau confirmed the results of the original study conducted by Feinblatt and Gant on the safety and efficacy of using a combination of alanine, glutamine, and glycine in the treatment of BPH. Damrau reported that he observed no side effects in the experimental group.

In 1978 Cuervo et al. studied the effects of the amino acid combination (alanine, glutamine, glycine) together with the herb, Prunus arboarea. They determined that the inclusion of the amino acids with the herb led to a considerable reduction in the duration of treatment for BPH patients resulting in significant financial savings. This study included 100 patients with prostate adenoma, prostatitis, and BPH.

In Japan, this amino acid combination is available as Paraprost for the treatment of BPH. Maekawa compared the effects of Paraprost with another drug, Cernilton, on BPH. This multicenter double blind study included 192 patients with BPH. The researchers determined that Paraprost (the amino acid combination) was more than moderately effective in 46.3% of the patients studied. Yamaguchi et al. (1980) also compared the effects of Paraprost with another drug (a selective alpha 1-adrenoreceptor blocker) in a double-blind multi-institutional study. They observed 77 patients with BPH and determined that Paraprost significantly improved obstructive and irritative symptoms, and reduced the incidence of residual urine.

The combination of these three amino acids — alanine, glutamine and glycine — offers favorable clinical results for the patient with BPH. The therapy appears to enhance the positive effects of herbal prostate medicines.
Zinc

The prostate gland has a unique characteristic of storing remarkably high levels of zinc. In fact, healthy prostate tissue contains a higher concentration of zinc than any other tissue in the human body. It is no coincidence that the level of zinc in the prostate gland declines dramatically in patients with BPH, and even more so in patients with prostate cancer. Zaicheck et al.\(^\text{65}\) studied 109 patients with BPH (50 cases) and prostate cancer (109 cases). The researchers used transrectal punch biopsy of prostate and radionuclide-induced energy dispersive X-ray fluorescent analysis to determine zinc concentrations in prostate tissue. They showed that the zinc content in cancerous prostate tissue was dramatically less than the concentration found in healthy prostate tissue. Specifically, zinc content of the normal prostate was 1018 micrograms/g dry tissue (M+/−124) compared to 146 M+/−10 in the cancerous prostate tissue. Costello et al.\(^\text{66}\) found an interesting correlation between citrate metabolism in the prostate, zinc accumulation, and prostate cancer. They determined that, in addition to zinc, the prostate accumulates and secretes exceptional levels of citrate from prostate epithelial cells. These cells will not secrete normal amounts of citrate if the zinc level in prostatic mitochondria drops. Specifically, the accumulation of zinc inhibits an enzyme that causes citrate oxidation. Thus, in patients with prostate cancer, as the level of zinc in the prostate drops, the threat of citrate oxidation increases. Perhaps the most interesting finding was that prolactin and testosterone regulate the concentration of zinc in the epithelial cells that produce citrate. Numerous medical researchers have made the correlation between zinc levels and BPH and cancer.\(^\text{56,67–71}\)

Despite this correlation, there has been little support for further investigation of the nutritional etiology of BPH and prostate cancer. It is also important to note that preliminary research suggests that over supplementation with zinc (over 100 mg per day) for prolonged periods may increase risk of prostate carcinogenesis. This is based on an epidemiological study\(^\text{72}\) where confounding variables exist, including concurrent high dose supplement intake of other ingredients such as calcium. Nevertheless, it does elucidate the point that more is not necessarily better with dietary supplement intake.

Tomatoes

Compared to other known carotenoids, lycopene is considered by experts to be one of the most potent antioxidants, with its unsurpassed singlet-oxygen quenching capacity. An impressive number of clinical trials and epidemiological studies demonstrate the statistically significant association between consumption of lycopene in foods, such as tomatoes and prostate health. However, most of the investigations are plagued by the uncertainties common to dietary therapeutics – the variability in food content of the agent under investigation, its isoforms, the multiple unknown interactions between the suspect chemical and the many other ingredients in the host food, influences of other dietary variables, and even the pharmacokinetics of the agent in the human body. Nevertheless, accumulated evidence to date supports a benefit from lycopene in one form or another, and more so when obtained from whole foods, in reducing the risk of prostate cancer.\(^\text{72}\)

Selenium

Selenium may have potent anti-cancer properties. Results from laboratory experiments suggest that selenium-enriched broccoli activates certain anti-cancer transcription pathways in mouse livers.\(^\text{74}\) Dog data suggest that dietary selenium supplementation decreases DNA damage and increases epithelial cell apoptosis within the aging canine prostate.\(^\text{75}\)

One of several prospective human selenium studies to show a positive effect on cancer was published in 1996 in JAMA.\(^\text{76}\) The researchers had originally chosen only skin cancer but included prostate, lung and colorectal seven years into the 13-year study because of positive results. The study included almost 1000 men from regions of the US with mean plasma selenium concentrations in the lower range of US levels. The double-blinded, randomized study gave 200 micrograms of selenium as brewer's yeast, or placebo, daily for 4.5 years and followed the subjects for an additional 6.4 years. Total cancer incidence (77 cases versus 119), prostate cancers (13 versus 35),...
colorectal cancers (8 versus 19), and lung cancers (17 versus 31) were all significantly lower in the selenium group than in the placebo group. There was no detectable increase in adverse effects from the supplementation. Because the study was small and not originally planned for the significant endpoints and the population was in the lowest range of selenium levels, it is considered preliminary and in need of verification. Nevertheless, it strongly suggests a beneficial and safe role for this supplement.

A population study carried out on 212 cases and 233 controls found a modest negative correlation between serum selenium levels and the incidence of prostate cancer.77 The inverse association with selenium was strongest among men with low serum concentrations of α-tocopherol, another antioxidant.

### Essential Fatty Acids

The body synthesizes some fat on its own, but there are also fats that the body is incapable of manufacturing known as “essential fatty acids” or EFAs. They are the omega 3 (alpha-linolenic) and omega 6 (linoleic) fatty acids. Essential fatty acids are required constituents of every membrane in the body. Classic signs of deficiency include depression, mood disorders, memory loss, hyperactivity, anxiety, dry flaking skin, inflammation, arthritic pain, bursitis, decreased bone density, easy bruising, muscle spasms, food allergies, fatigue, increased body fat, sub-clinical and clinical hypoglycemia, hormonal imbalance, and dry hair. EFAs are required to maintain the health of every living cell in the body. They maintain the fluidity of cellular membranes, aid in producing and balancing hormones, and play an essential role in managing inflammation. From essential fatty acids the body produces many compounds including a group of components known as prostaglandins.

Interestingly, the word prostaglandin comes from the fact that these products of fatty acid metabolism were originally found in the prostate gland (prosta - gland - in). Prostaglandins regulate every organ system in the body. One essential rate-limiting enzyme in the transformation of EFAs into the important prostaglandins is 6- desaturase. Interestingly, zinc deficiency blocks this enzyme. Other factors that block this enzyme include trans fatty acids, vitamin B3 and B6 deficiencies, toxic chemicals, alcohol, and some viruses.

A study conducted by medical researchers in Korea established a connection between BPH, prostate cancer, and essential fatty acids. Yang et al.78 examined the role of dietary fatty acids in benign and malignant prostate disease by comparing serum fatty acid levels in normal controls, patients with prostate cancer, and patients with BPH. They also looked at the relative difference in omega 3/omega 6 fatty acid ratios between the three groups. The omega 3/omega 6 fatty acid ratios decreased progressively from control (largest fraction) to BPH to prostate cancer (lowest fraction) indicating that BPH patients have less omega 3 fatty acids in their serum, and prostate cancer patients have significantly less omega 3 fatty acids in their serum. This is a landmark study, as it makes a direct correlation between omega 3 fatty acid deficiencies and prostate disease (BPH and cancer).

Researchers are still not clear on what the entire purpose of the prostate gland is and the extent of its functions. What the medical community does know is that it is a critical gland of the male reproductive system and that when this gland is diseased in any way, it can cause a tremendous amount of pain and suffering for the male patient. After reviewing the various conditions associated with prostate disease, including benign prostatic hyperplasia (BPH), prostatitis, and even cancer, and examining the standard lines of treatment for these conditions, herbal and nutrient medicines appear to be an important primary or complementary therapy for the male patient experiencing sub-optimal prostate health.

### References

10. Williams RM. Environmental clues to prostate cancer. TLDPEP 1999;11:144-146.
Natural Therapies for Prostate

For Temporary Relief of Occasional Indigestion and Heartburn*

GES-5 is a combination of nutrients designed to provide relief of intermittent heartburn and indigestion.*

Alginic acid and sodium alginate react with saliva and gastric acid to form a foamy froth or "alginic raft" that floats on top of the gastric contents and prevents acid and food reflux from re-entering the esophagus.* Slippery elm and deglycyrrhizined licorice act as demulcents which are soothing to the alimentary canal.*

For more information about our full product line or to place an order call:

1-800-792-2222

Rx Vitamins

Physician Formulated

Scientifically Advanced Nutritional Supplements

visit us at www.rxvitamins.com • email: info@rxvitamins.com

* This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

TOWNSEND LETTER for DOCTORS & PATIENTS – AUGUST/SEPTEMBER 2004

75