PROSTATE SUPPORT:

GRAMINEX Flower Pollen Extract

Use of natural products to treat benign prostatic hyperplasia (BPH) and chronic non-bacterial prostatitis: emphasis on Cernitin®

By Harry G. Preuss, MD FACN CNS

Professor of Medicine and Pathology

Georgetown University Medical Center- Washington DC

Many males throughout the world, both young and old, suffer severely from the ravages of cardiovascular disorders and cancers, but another important area of specific concern receiving less attention involves a small gland of the reproductive tract called the prostate [1]. The prostate is very important for a number of health reasons. Malignancy of this gland is recognized as the most common cancer among men (1 out of 10) and, unfortunately, is the second most fatal. It has been estimated that over 300,000 men will develop prostate cancer in the coming year, and more than 40,000 will succumb to it. It is important to note that the prostate gland is also the origin of an even more widespread problem – benign prostatic hyperplasia surpasses that of prostatic cancer – nearly 60% of men over the age of 40 have an enlarged prostate, and the incidence increases to over 80% by the age of 80 [2-5]. Over $1 billion dollars are spent each year on treatment for prostatic enlargement.

The major function of the prostate, a gland associated with the male reproductive system, is to produce and discharge a various alkaline liquid that provides a major portion of the seminal fluid. This gland is made up of both muscular and glandular tissue. It produces semen to carry sperm in the ejaculate. Sperm are protected, at least to some extent, and can survive longer after ejaculation because of the environment afforded by the presence of prostatic fluid. Prostatic fluid also contains prostaglandins, which are fatty acids that, similar to hormones, affect smooth muscle fibers and blood vessel walls.

Although the prostate plays no direct role in the functioning of the male urinary system, many urinary perturbations occur when it expands via growth due to its location at the outlet of the bladder [1,6]. The prostate is located in front of the rectum and below the urinary bladder. Importantly, it surrounds the urethra, a tube which carries urine from the bladder to the tip of the penis for expulsion. The gland is the size of a pea at birth and grows slowly until puberty. Driven by sex hormones, the prostate grows at a faster pace. During the 20s and 30s, the gland is characteristically the size of a walnut, weighing roughly one ounce. Around age 45, cells in the prostate multiply once more causing the gland to grow up to 10 times the normal adult size [7].

Common symptoms of obstructive BPH include (1) a weak urinary stream, (2) a sense of incomplete bladder emptying, (3) difficulty initiating urination, (4) frequent urination (especially at night when it is referred to as nocturia), (5) urgency (difficult postponing urination), and (6) interruption of the stream (stopping and starting). The typical sufferer usually becomes aware of the problem when the urge to urinate becomes more frequent than expected. The person suffering from BPH rarely can sit through a movie or concert – he is the one that requests the aisle seat on an airplane in order not to disturb his fellow passengers by his

frequent sojourns to the restroom. At night, trips to the bathroom caused by nocturia steadily increase, so that there is a definite impingement on sleep. Accordingly, any experiencing of such urinary frequency should lead to suspicion of the disorder. In view of the rising life expectancy of the male population, knowledge of the means with the best risk/ benefits ratio to treat BPH in its various stages will become more important.

In the past, treatment options for prostate enlargement focused on surgery. Over the last few years, prescription drugs have been used to initiate therapy against BPH in its early stages. One highly recognized group of agents works chiefly to inhibit the activity of 5-alpha reductase (finasterides). Another group works to relax the muscle tissue of the prostate and thus relieve the pressure around the urethra (alpha blockers). Unfortunately, surgery and pharmaceuticals used to treat BPH carry a high cost and the added risk of potentially debilitating side effects. In recent years, emphasis has been placed upon the use of natural compounds to ameliorate the symptoms of BPH and chronic non-bacterial prostatitis. The attractiveness of natural compounds, for the most part, lies in their fewer serious side effects compared to drugs. In many cases, natural products work similar to many pharmaceuticals used to treat BPH. Some plant extracts not only lower the rate of DHT formation like finasterides, but block the ability of DHT to bind to cells, preventing the action of hormone. They may also relax the musculature involved in urination similar to alpha blockers. In addition, they may prevent severe inflammatory responses similar to drug inhibitors of the prostaglandin cascade (COX 2 inhibitors).

A number of natural products have been recognized as having some therapeutics use for prostate problems. The natural product most used for prostate problems is saw palmetto [8-13]. A number of clinical studies have substantiated the efficacy of saw palmetto usage in treating BPH [14-19]. *Pygeum africanum* contains phytosterols which have been purported to have anti-inflammatory properties [20]. When 263 German men were tested with *Pygeum africanum,* urinary symptoms improved in 66% compared to 31% in the placebo group. Occasional gastrointestinal upset seems to be the major adverse side effect.

Less work has been performed using the stinging nettle (Urtica dioica) to ameliorate BPH [21,22]. Of late, much attention has been focused on beta-sitosterol [23]. Beta-sitosterol is a phytopharmacological agent containing many phytosterols. In a randomized, double-blind study reported in the Lancet [24], 200 patients with symptoms of BPH from eight private urological practices were treated for six months with either 20 mg of beta-sitosterol or placebo. At the end of six months, modified Boyarsky scores [25] decreased significantly in the beta-sitosterol treated group compared to placebo. Reduction took place in prostatic volume, the quality of life score improved, the peak urine flow increased, and the mean voiding time and urinary volume retention also improved from the initial scores in the sterol group, whereas no changes were noted in the placebo group. Importantly, no severe adverse reactions were attributed to beta-sitosterol.

Compared to other natural products, a defined flower pollen extract called “Cernitin” has received less recognition in the USA as a therapeutic agent for prostate perturbations [26]. Ironically, it may be the best natural product for this condition yet recognized. In 1950, a beekeeper in a tiny Swedish village found a way to collect pollen artificially [27]. Initially, the flower pollen was used as a prophylactic agent against infections. Later the extraction process was modified so that the active pollen was released and was non-allergenic. Oily Cernitin GBX and water soluble Cernitin T60 are important extracts of a mixture of three different pollen strains: timothy, maize, and rye. Found in the pollen are peptides, carbohydrates, fatty acids, vitamins, minerals, nucleic acids, and enzymes. Whatever the original hypothesis concerning overall health, Cernitin proved specifically useful in treating BPH [28].

Many types of clinical trials of all varieties examining the therapeutic benefits of Cernitin on prostate perturbations, including randomized, multi-center, double-blinded, and placebo-controlled, have been published. The most significant investigations have been performed in Europe (Germany, Britain, Switzerland) and Japan. End points for examination have included both subjective (various questionnaires and history of symptom amelioration) and objective (flow rates, residual urine volumes, estimation of prostate size, and concentration of prostatic specific antigen [PSA evaluation]) criteria. The overall trend in all these trials, both open and blinded, was to show an improvement in the symptoms and signs of BPH and chronic prostatitis, whether subjective and/or objective criteria were used. Following are brief descriptions of some clinical investigations:

1. Using pollen extract, Leander [29] found a 60-80% improvement over placebo in symptoms of obstruction, probably through elimination of inflammatory edema.
2. In 1967, Ohkoshi, Kawamura and Nagakubo of Keio University, reported impressive results in 30 patients with prostatitis and/or urethritis [30]. Examining 14 patients receiving Cernitin, it was found that treatment was successful in 10, slightly effective in three, and ineffective in only one case.
3. Takeuchi [31] investigated both subjective and objective effects on Cernitin on 25 men with BPH. There was a 50% improvement of nocturnal micturition.
4. Inada et al., reported favorable effects in 12 patients suffering from prostatic hypertrophy [32]. They reported that five cases had “effective” results, five showed “slightly effective” results and two reported “ineffective” results.
5. In 1986, a field study of 2,289 patients being treated by 170 urologists was undertaken [33]. Improvement of symptoms was reported in 64-82%, in contrast to a low rate of adverse reaction found only in 2.9% of cases.
6. Brauer [34] compared the effects of Cernitin and beta-sitosterol in 39 patients. A significant reduction in circulating levels of PSA with Cernitin therapy indicated a reduction of cell lesions in BPH. In contrast, no such change occurred with beta-sitosterol treatment. Although flow pollen extract proved superior to beta-sitosterol in many respects, the mean values for residual urine volume fell under 15 ml for both at the end of the treatment.
7. In a double-blind, placebo-controlled study performed in 1988 in collaboration with six practicing urologists, Becker and Ebeling examined 48 patients taking Cernitin and compared them with an equal number of patients receiving placebo over a 12-week interval [35]. The results showed that there was a significant improvement using Cernitin compared to placebo of nocturia, i.e., 69% vs. 37% ($p<0.005$). Not only the sensation of residual urine but the actual volume of residual urine was significantly reduced by flower pollen extract. Mild nausea was reported in one patient.
8. In a follow-up, open study emanating from the above double-blinded study, 92 patients, all receiving Cernitin, were evaluated [36]. There was a marked improvement in nocturia and residual urine volume. Differences between Cernitin and placebo groups during the initial double-blind phase were balanced out after the switch from the placebo to Cernitin.
9. In an open trial using the defined Cernitin pollen extract on 15 patients with chronic prostatitis or prostadynia, Buck and his colleagues reported that 13 obtained either complete and lasting relief of symptoms or marked improvement – only two patients failed to respond [37].
10. In a paper appearing one year later, Buck, et al., performed a larger study on 57 patients with outflow obstruction due to BPH [38]. This was double-blind, placebo-controlled trial to evaluate the effect of a six-month course of pollen extract on symptomatology. The overall subjective improvement with the defined Cernitin pollen extract of 69% more than doubled that of the placebo group (30%). The investigators reported a significant decrease in residual urine with Cernitin and in the antero-posterior diameter of the prostate by ultrasound assessment.
11. Rugendorff, et al. [39], performed a prospective, case-controlled, open trial to treat chronic prostatitis and prostadynia. In 90 patients who were treated for six months,

freedom of symptoms and normalization of the palpation finding were obtained in 50-70% of patients without complicating factors.

12. Braun and Peyer [40] in a 1993 double blind, placebo-controlled investigation on 44 patients with Grade I and II BPH assessed the validity of treatment with flower pollen extract on subjective and objective parameters. They found by using questionnaires, echography, and laboratory analysis of PSA that flower pollen extract had a clear benefit over placebo. In 25 patients receiving verum compared to 19 receiving placebo, there was a significant reduction in the mean number of both diurnal and nocturnal micturitions with flower pollen extract ($p<0.05$). Using ultrasonic measures, the mean volume of the prostate decreased significantly more in the verum group (-29% vs -8.8%, $p<0.05$). More reduction in residual urine volume and PSA levels were noted in the verum group.
13. An open post-marketing observation study in which 208 doctors participated investigated the efficacy and tolerability of Cernitin in the treatment of BPH stage I-II according to Aiken [41]. One thousand seven hundred ninety-eight patients were treated for 24 weeks. Improvements in all irritative symptoms in 50-80% were noted, and residual urine volume improved. Adverse effects were noted in 15 patients (0.8%). The perturbations were mainly gastrointestinal symptoms, and termination of treatment because of adverse effects was seen only in four patients.
14. In Japanese study published 1995, 79 patients were treated with Cernitin pollen extract [42]. At a dosage of 126 mg tid, symptom scores based on a modified Boyarsky rating scale [25], uroflowmetry, prostate volume, and residual volume were measured. Urine maximum flow increased significantly from 54.2 ml to less than 30.0 ml. When 28 patients who had received treatment for one year were examined, a mean decrease of prostatic volume of 26.5 cm3 was found.

We undertook a randomized, placebo-controlled, double-blind study using a combined treatment of Cernitin, saw palmetto, vitamin E and beta-sitosterol [43]. Patients were enrolled from 3 urological practices in the USA. One hundred forty-four subjects were randomized for study. Patients received either placebo or the combined natural products for 3 months. Evaluations were performed via the AUA Symptom Index scores, urinary flow rates, PSA measurements, and residual bladder volumes. Nocturia showed a markedly significant decrease in severity in patients receiving the combined natural products compared to those taking placebo ($p<0.001$). Daytime frequency was also lessened significantly ($p<0.04$). When the average individual total AUA Symptom Index score in the verum group was compared to that in the placebo group, the difference proved highly significant ($p<0.014$). PSA measurements, maximal and verage urinary flow rates, and residual volumes showed no statistically significant differences.

The major mechanism behind the beneficial action of Cernitin is believed to be inhibition of edema formation and prevention of inflammation in the prostate. Inflammation of the prostate can cause edema of the interstitial tissue surrounding the acini and ducts of the glands leading to poor drainage. This, in turn, creates difficulty in voiding, dysuria, frequency, and nocturia – symptoms which have been shown to improve with flower-pollen extract usage. In addition, pollen extract has been reported to reduce prostatic volume and residual volume, and improves voiding difficulties and urinary flow rates of patients with BPH. Obviously, pain may be due to such processes and will remit if these perturbations are overcome. It is believed that the anti-congestive action is based upon the inhibition of prostaglandin and leukotriene and cyclo-oxygenase enzymes are markedly reduced and the arachidonic cascade is interrupted [28].

Additional pharmacological effects reported for the pollen are: inhibition of prostate cell growth in animals, influences on contractibility of bladder and urethral smooth muscle, as well as diaphragms of animals, and influences on metabolism of dihydrotestosterone [28]. In conclusion, the combined mechanisms behind

the effects of Cernitin pollen extract will go a long way to ensure overall prostate health.

References

1. Salcedo H. The Prostate. Facts and Misconceptions. Birch Lane Press Book: New York, 1993.
2. Jacobsen SJ, Griman DJ, Guess HA, et al. “New Diagnostic and Treatment Guidelines for Benign Prostatic Hyperplasia. Potential Impact in the United States.” Arch Int Med, 1995; 155:477-481.
3. Berry SJ, Coffey DS, Walsh PC, and Ewing LL. “The development of human benign prostatic hyperplasia with age.” J Urol, 1994; 132:474-479.
4. Lytton B, Emery JM, and Howard BM. “The incidence of benign prostatic hypertrophy.” J Urol, 1968; 99:639-645.
5. Knott MA and Bootman JL. “The economics of benign prostatic hyperplasia treatment: a literature review.” Clinical Therapeutics, 1995; 18:1227-1241.
6. Oesterling JE. “Benign prostatic hyperplasia: a review of its histogenesis and natural history.” The Prostate Supplement, 1996; 6:67-73.
7. Buttyan R, Chen M-W, and Levin RM. “Animal model of bladder outlet obstruction and molecular insights into the basis for the development of bladder dysfunction.” European Urology, 1997; 32 (Suppl 1):32-39.
8. Breu W, Stadler F, Hagenlocher M, and Wagner H. “Der sabalfrucht-extrakt SG 291. Ein phytotherapeutikin zur behandlung der benignen prostatahyperplasie.” Zeitschrift Fur Phtyotherpie, 1992; 13: 107-115.
9. Brue W, Hagenlocher M, Redl K, et al “ Antiphlogistische wirkung eines mit hyperkritischem kohiendixid gewonnenen sabalfrucht-extraktes.” Arzneim Forsch Drug Research, 1992; 42: 547-551.
10. Stenger A, Tarayre JP, and Carilla F. “Etude pharmacologique et biochimique de l’extrait hexanique de Serenoa repens.” B Gaz Med de France, 1982; 89:2041-2048, 1982.
11. Rhodes L, Primka RL, Berman C, et al. ”Comparison of finasteride (Proscar), a 5a reductase inhibition.” The Prostate, 1993; 22: 45-51.
12. Sultan C, Terraza A, and Divillier C. “Inhibition of androgen metabolism and binding by a liposterolic extract of Serenoa repens B in human foreskin fibroblasts.” J Steroid Biochem, 1984; 20: 515-521.
13. Carilla E, Briley M, Fauran F, Sultan C, and Duvilliers C. “Binding of Permixon, a new treatment for prostatic benign hyperplasia, to the cytostolic androgen receptor in the rat prostate.” J Steroid Biochem, 1984; 20:521-523.
14. Champault G, Patel JC, and Bonnard AM. “ A double-blind trial of an extract of the plant Serenoa repens in benign prostatic hyperplasia.” Br J Clin Pharmacol, 1984; 18:461-462.
15. Carraro JC, Raynaud JP, Koch G, et al. “Comparison of phytotherapy (Permixon) with finasteride in the treatment of benign prostate hyperplasia: a randomized international study of 1,098 patients.” The Prostate, 1996; 29: 231-240.
16. Posker GL and Brogden RN. ”Serenoa repens (Permixon). A review of it pharmacology and therapeutic efficacy in benign prostatic hyperplasia.” Drug and Aging, 1996; 9:379-395.
17. Denis LJ. Editorial review of “Comparison of phytotherapy (Permixon) with finasteride in the treatment of benign prostatic hyperplasia: a randomized international study of 1,098 patients.” The Prostate, 1996; 29:241-242.
18. Braeckman J. “The extract of Serenoa repens in the treatment of benign prostatic hyperplasia: a multi center open study.” Curr Therap Res, 1994; 56:776-785.
19. Champault G, Bonnard AM, Cauquil J, and Patel JC. “Medical treatment of prostatic adenoma. Controlled trial PA 109 vs placebo in 110 patients.” Ann Urol, 18:407-410.
20. Bartlet A, Albrecht J, Aubert A, et al. “Efficacy of Pygeum africanum extract in the medical therapy of urination disorders due to benign prostatic hyperplasia: evaluation of objective and subjective parameters. A placebo-controlled double-blind multicenter study.” Wiener Klinische Wochenschrift, 1990; 102: 667-673.
21. Lichius JJ and Muth C. “The inhibiting effects of urtica dioica root extracts on experimentally induced prostatic hyperplasia in the mouse.” Planta Medica, 1997; 63:307-310.
22. Hirano T, Homma M, and Oka K. “Effects of stinging nettle roots and their steroidal components on the Na+, K+ ATPase of the benign prostatic hyperplasia.” Planta Medica, 1994; 60:30-33.
23. Klippel KF, Hilti DM, and Schipp B. “ A multi center, placebo-controlled, double-blind clinical trial of beta-sitosterol (Phytosterol) for the treatment of benign prostatic hyperplasia.” BR J Urol, 1997; 80:427-432.
24. Berges RR, Windeler J, Trampisch HJ, et al. ”Randomized placebo-controlled clinical trial of B-sitosterol in patients with benign prostatic hyperplasia.” The Lancet, 1995; 345:1529-1532.
25. Boyarsky S, Jones G, Paulson DF, et al. “ A new look at bladder neck obstruction by the Food and Drug Administration regulators: guide lines for investigation of benign prostatic hypertrophy.” Transactions of the American Medical Association of Genito-Urinary Surgeons, 1977; 68:29-32.
26. Preuss HG and Adderly B. The Prostate Cure. Crown Publishers, Inc: New York, NY, 1998: 1-251.
27. Asplund A. Searching for the source of life and vitality. Sanomin (SA) SDN: Singapore, 1991:36.

28. Loschen G and Ebelin L. " Hemmung der arachindonsaure-kaskade durch einen extrakt aus roggenpollen."
29. Leander G. "A preliminary investigation on the therapeutic effect of Cernilton N in chronic prostatovesiculitis." Sveska Lakartidningen, 1962; 59:3296.
30. Ohkoshi M, Kawamure N, and Nagakubo I. Japanese Journal of Urology, 1967; 21:73.
31. Takeuchi H, et al. "Quantitative evaluation on the effectiveness of Cernilton on benign prostatic hypertrophy." Hinyoki Kiyo, 1981;27.
32. Inada T, Kitagawa T, and Miyakawa M. Use of Cernilton in patients with prostatic hypertrophy. Tobishi Pharmaceutical Co, Ltd: Tokyo, Japan, 1966.
33. Ebeling L. "The therapeutic result of defined pollen extract in patients with chronic prostatitis. In: Schmiedt E, Alken JE, Bauer HW (eds). Therapy of Prostatiits. Zuckschwerdt Verlag: Munchen, 1986: 154-160.
34. Brauer H. "The treatment of benign prostatic hyperplasia with phytopharmacia: a comparative study of Cernilton and beta sitosterol." Therapiewhoche, 1986; 36: 1686-1696, 1986.
35. Becker H and Ebeling L. "Conservative treatment of benign prostatic hyperplasia (BPH) with Cernilton N. Results of a placebo-controlled double-blind study." Urologe B, 1988; 28:301-306.
36. Becker H and Ebeling L. "Phytotherapy of BPH with Cernilton N. Result of a controlled clinical study." Urologe B, 1991; 31:113-116.
37. Buck AC, Cox R, Rees RWM, and Ebeling L. "Treatment of chronic prostatitis and prostadynia with pollen extract." Br J Urol, 1989; 64:496-499.
38. Buck AC, Cox R, Rees RWM, et al. "Treatment of outflow tract obstruction due to benign prostatic hyperplasia with the pollen extract, Cernilton. A double-blind, placebo-controlled study." Br J Urol, 1990; 66: 398-404.
39. Rugendorff EW, Weidner W. Ebeling L, and Buck AC. " Results of treatment with pollen extract (cernilton N) in prostadynia and chronic prostatitis." Br J Urol, 1993; 71:433-438.
40. Braun L, Peyer P, Ackermann, et al. "A multicenter, placebo-controlled study on the efficacy and tolerability of adenoprostal in patients with benign prostatic hyperplasia (BPH)." Tribuna Medica Ticinese, 1993.
41. Bach D and Ebeling L." Possibilities and limitations of phytotherapy for benign prostatic hyperplasia (BPH): results of treatment with Cernilton N for stages I-II according to Alken (or II-IV according to Vahlensieck)." In: Benign Prostatic Diseases. W Vahlensieck, G Rutishauser (eds). Georg Thieme Verlag: Stuttgart, Germany, 1992: 180-187.
42. Yasumoto R, Kawanishi H, Tsujino T, et al. "Clinical evaluation of long-term treatment using Cernitin pollen extract in patients with benign prostatic hyperplasia." Clinical Therapeutics, 1995; 17:82-87.
43. Preuss H, Marcusen C, Regan J, Klimberg I, Welebir T, and Jones W. "Randomized trial of a combination of natural products (Cernitin, saw palmetto, b-sitosterol, vitamin E) on symptoms of benign prostatic hyperplasia(BPH)," J Am Coll Nutr, 1999; 18: 534 (abstract).