A Critical Review of Cernitin™ for Symptomatic Relief of Lower Urinary Tract Symptoms (LUTS) in Men

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Objective

We reviewed published data concerning the ability of a defined flower pollen ex-tract derived from rye, corn, and timothy, commonly referred to as Cernitin to provide symptomatic relief in men suffering from lower urinary tract symptoms (LUTS). This same defined pollen extract has also been called Cernilton in other reports and is commercially available as Graminex Flower Pollen Extract. To maintain clarity, however, we will only use the term Cernitin to describe the defined pollen extract. In writing this review, our major goal is to present evidence concerning the therapeutic role of Cernitin in the management of mild to moderate LUTS. Nevertheless, we briefly describe prostatic perturbations in general and other natural therapeutic approaches to alleviate symptoms caused by them.

Introduction

It is estimated that 9-10 million men have lower urinary tract symptoms (LUTS) secondary to an enlarged prostate; and 400,000 surgeries are conducted each year in the U.S to alleviate such symptoms [1,2]. Although cancer might be a root cause, LUTS are more commonly found in men with non-cancerous conditions such as benign prostate hyperplasia (BPH), prostadynia, acute and chronic prostatitis caused by a bacterial infection, as well as chronic non-bacterial prostatitis. BPH, the most common cause of LUTS, does not distinguish between race and ethnic background, although African-American men are at a slightly greater risk [3]. It does not relate to sexual activity, since it can occur in celibate priests as well as the most sexually active of men [4]. Regardless of the etiology of the specific prostate-related disorders, health worries associated with prostatic enlargement are significant. Over $1 billion dollars are spent each year on treatment for prostatic enlargement, because LUTS can lead to more serious health problems if not treated properly [5].

The term LUTS describes men experiencing one or more symptoms listed on the International Prostate Symptom Score (IPSS) questionnaire. Among the mentioned urinary symptoms are daytime and night time (nocturia) frequency, urgency, hesitancy, intermittency, sensation of incomplete voiding, and decreased force of urinary stream [2]. An individual often becomes aware of the problem when urination occurs more frequently than usual. He may eventually become the person who rarely can sit through a movie or concert -- the one that requests the aisle seat on an airplane so as not to disturb his fellow passengers on his frequent sojourns to the restroom. At night, the trips to the bathroom caused by nocturia steadily increase, and there is a definite impingement on sleep. Suffice it to say, any experiencing of such frequency should lead to suspicion of the disorder.

What do we know about this troublesome gland? The prostate gland is associated with the male reproductive system. Its major function is to produce and discharge a viscous, alkaline liquid that provides a major portion of the seminal fluid. The prostate makes and stores fluid almost continuously. Because of the environment afforded by the presence of prostatic fluid, sperms are protected, at least to some extent, and can survive longer after ejaculation. In addition, the prostatic fluid 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, its location near the bladder and urethra cause many urinary perturbations when it expands via growth or response to chronic inflammation [6-8].

At birth, the gland is the size of a pea and grows slowly until puberty. Under the influence of sex hormones, the prostate grows at a faster pace. During the 20's and 30's, the gland is characteristically the size of a walnut and weighs roughly one ounce. The gland, made up of muscular and glandular tissue, is located in front of the rectum and below the urinary bladder. Importantly, the gland surrounds the urethra, a tube that carries urine from the bladder to the tip of the penis for expulsion. Obviously, this setting has the potential to cause problems and unfortunately does. Around the age of 45, cells in the majority of prostates began to multiply again and the gland can reach up to 10 times the normal adult size [3].

The prostate can be divided into various lobes, with the major problems of BPH lying in the small transitional zone. The transitional zone that lies within the so-called middle lobe is the sole site of BPH [9]. Interestingly, the small transition zone comprises only two per cent of the entire prostatic mass before enlargement. Obviously, enlargement of this area does not in itself increase the size of the prostate greatly. Because of this, the degree of urethral obstruction may not directly relate to the overall size of the prostate gland but instead to the direction of growth enlargement. Some men with greatly enlarged prostates may have no signs of obstruction, while those with relatively small prostates may have severe obstruction.

While the exact mechanism behind age-related enlargement of the prostate is uncertain, a highly active form of the male hormone, testosterone, called dihydrotestosterone (DHT), is considered a major factor behind prostatic enlargement [4]. Excessive levels of DHT have been found in men with enlarged glands, and high concentrations of DHT are also associated with an increased risk of prostate cancer. To make matters worse, the concentration of DHT within the prostate increases with age. A major factor in the rise is that the enzyme responsible for the conversion of testosterone to DHT, 5-alpha reductase, becomes more active over the lifespan. Therefore, it is not too surprising that 5-alpha reductase is an important focal point in the medical treatment of prostate enlargement. Nevertheless, it is equally important to be aware that other prostatic enzymes, such a 3 oxidoreductase, deficiency of minerals such as zinc, and inflammation may also play a role in the enlargement process.

Background of Treatment

Bruskewitz points out that since serious complications from BPH and related non-cancerous conditions are rare, the primary aim of pharmacological treatment is to improve quality of life by relieving the vexing symptoms [10]. Studies conducted in the U.S. showed that urologists provided no specific treatment 77% of the time to men with mild symptoms. With moderate symptoms, however, prescription drugs were given 89% of the time; and surgery was conducted 1% of the time. The primary therapeutic treatment was use of alpha (1)-adrenoceptor antagonists such as terazosin hydrochloride (Hytrin®) that provide symptomatic relief but have not been shown to influence the incidence of surgery, acute urinary obstruction, or other complications of BPH [11]. In the past, treatment options for significant prostate enlargement focused on surgery. In a given year, approximately 400,000 men are driven to undergo a procedure called a transurethral resection of the prostate (TURP). Even now, transurethral resection is the standard treatment for BPH, i.e., the gold standard by which all other procedures are measured [12]. Unfortunately, while many symptoms of obstruction are ameliorated, post urination dripping may continue and may even result in severe incontinence. Even worse, the operation may be followed by a decline in sexual function. This may also occur with the use of the common pharmaceuticals as well [2]. Accordingly, a need exists for safe, effective products that can be used to treat mild

to moderate LUTS in lieu of or in addition to prescription drugs and major surgery. Natural products have been considered among the alternative therapies.

Natural Products to Treat LUTS

Saw Palmetto (Serenoa Repens)

Research carried out in Europe over the past 20 years shows that natural, fat-soluble extracts from specific plants effectively inhibit the function of 5-alpha-reductase, and block, at least in part, the formation of DHT [13-16]. The best-known and most extensively researched plant is saw palmetto. Saw palmetto is an extract of the pulp and seeds of a dwarf, scrubby palm tree native to the West Indies and the Atlantic coast of the United States. Saw palmetto works, for the most part, by the same mechanism as the pharmaceutical Proscar®, i.e., preventing the conversion of testosterone to DHT [16]. Additional benefits from plant extracts have also been found and may add to the good results found with their use. Some plant extracts not only lower the rate of DHT formation, but also block the ability of DHT to bind to cells, preventing the action of hormone [17,18]. In addition, they may prevent severe inflammatory responses. Saw palmetto, known to be popular in Europe, has recently become recognized in America. In one study using saw palmetto in 110 men, it decreased nighttime urination by 45 percent, increased urinary flow rate more than fifty percent, and reduced the amount of urine left in the bladder after urination by 42 per cent [19]. In other large trials, improvement in prostatic symptomatology was readily noted and saw palmetto even compared favorably with Hytrin and Proscar when they were compared head to head [20-24].

Pygeum Africanum

The powdered bark of the pygeum tree, a large tropical African evergreen, has been used for centuries to treat urinary disorders [25]. Pygeum contains phytosterols, which have been purported to have anti-inflammatory properties. In addition, much benefit has been attributed to their ability to decrease prostatic swelling, to reduce harmful prostaglandins that induce inflammation, and to diminish circulating prolactin that decreases the prostate uptake of testosterone. When 263 German men were tested with Pygeum africanum, urinary symptoms improved in 66% compared to 31% in the placebo group [26]. Occasional gastrointestinal upset seems to be the major adverse side effect.

Stinging Nettle (Urtical dioica)

Less research has been performed using the stinging nettle to ameliorate BPH. Laboratory studies have shown its ability to inhibit laboratory induced prostate growth in mice [27]. The results from one study suggest that the steroidal components of stinging nettle roots suppressed prostate cell growth [28].

Beta-sitosterol

Much attention has recently been focused on beta-sitosterol. In a randomized double blind study reported in the Lancet, 200 patients from eight private urological practices were treated for six months with either 20 mg of beta-sitosterol or placebo [29]. At the end of six months, modified Boyarsky scores decreased statistically in the beta-sitosterol treated group compared to placebo. The quality of life score improved, the peak urine flow increased, the mean voiding time and the urinary volume retention also improved from the initial scores in the verum group, whereas no changes were noted in the placebo group. Results were also positive in another randomized, double-blind and placebo-controlled study carried out in Germany [30].

Cernitin

Cernitin is a natural product recently introduced in the USA to be used to treat LUTS. However, it has actually been around a long time. In 1950, in a tiny Swedish village, a beekeeper found a way to collect pollen artificially [31]. Since it was good for bees, his hypothesis was that it would be good for humans. 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. Found in the pollen are peptides, carbohydrates, fatty acids, vitamins, minerals, nucleic acids, and enzymes. Whatever the original hypothesis concerning overall health, the defined pollen extract called "Cernitin" proved specifically useful in treating BPH and other prostate conditions [2,32].

Cernitin is a standardized extract of rye pollen (*Secale cereale)*, corn pollen (*Zea mays),* and

timothy pollen (*Phleum pratense).* From these combined pollens, two important, therapeutic extracts are derived -- a water-soluble fraction and a lipid-soluble fraction with different physiological functions. *In vitro* and *in vivo* animal studies [33,34] have shown that both fractions have anti-inflammatory properties emanating from inhibition of prostaglandin and leukotriene synthesis. The water-soluble fraction has been shown to reduce the size of the ventral and dorsal prostate in the rat [35] and to inhibit testosterone-induced BPH in castrated animals [8]. The combined extracts were shown to inhibit growth of transplanted human BPH tissue in an athymic nude mouse model (36). Both fractions have been shown to relax the smooth muscle of the mouse and pig urethra, increase bladder muscle contractions [34], and reduce prostate size in mature Wistar rats [37].

Cernitin extracts are also sold as Graminex Flower Pollen Extract and are available in the marketplace in tablet and capsule forms, usually contain 63 mg of a 20:1 ratio of water-soluble to lipid-soluble fractions. Cernitin is contained in products regulated as drugs in Switzerland, Germany, Austria, Japan, South Korea and South Africa. In the U.S., the use of botanicals for LUTS is relatively less. No botanicals are approved as prescription or over-the-counter drugs for LUTS or BPH in the U.S. Accordingly, they are sold as dietary supplements and are labeled with non-specific information, e.g., "maintains prostate health." In a study conducted in Chicago in 1997-1998 with 738 men having LUTS and/or prostate disease, Bales et al [38] found that 13% of the group had used botanicals for their condition (59% in combination with prescription drugs), 37% were aware of botanicals as an option but had never used them, and 50% were unaware of this treatment option. Such information prompted our review of Cernitin.

Methods

Literature searches were conducted on Medline and the Cochrane Library. Sources such as review articles and monographs in botanical reference books and other books referring to Cernitin were included in the analysis. Open label and comparative trials were included in the assessment, although more weight was given to placebo-controlled, double-blind studies. Emphasis was placed on subject ratings of symptoms in light of the potential for self-medication of this extract.

Results

Reviews, Books, and Monographs

Four reviews [39-43] and a number of books/monographs [2,44-46] dealing largely with the clinical efficacy and safety of Cernitin have been published in recent years. Each used its own criteria to select studies considered to be valid. Because all reviews concluded that Cernitin is very safe with few or no side effects, the summaries described below are essentially limited to efficacy.

In the first, Commission E, an expert committee established by the German government to evaluate the safety and efficacy of over 300 botanical and botanical combinations sold in Germany, concluded in 1994 that combining extracts of rye, corn, and timothy pollen was useful in the treatment of "micturition difficulties associated with Alken stage I-II benign prostatic enlargement (BPH)" [39]. In the second, the Natural Medicines Comprehensive Database concluded that rye grass pollen extract (Cernitin) was "possibly effective" for the management of BPH symptoms, for shrinking prostate size, and for prostatitis and prostadynia based on the information it gathered [40]. In the third source, the same group published reviews in 1999 and 2000 based upon results from 4 double-blind studies (444 men in total, 2 studies with placebo; 2 with active controls) [41,42]. Results consistently showed a "modest" improvement in subjective symptoms and nocturia in the Cernitin groups compared to placebo, Paraprost (a mixture of the amino acids L-glutamic acid, L-alanine, glycine) and Tadenan (Pygeum africanum extract). The authors called for additional studies to evaluate long-term effects. In the final review, Shoskes concluded that there was credible clinical and scientific evidence that treatment with Cernitin pollen extract was efficacious for the majority of patients with non-bacterial prostatitis and prostadynia [43]. The books/monographs largely corroborate the conclusions of the reviews [2,44-46].

Research Papers

Again, Cernitin was well tolerated in all of the published studies from primary literature with minimal reported side effects. Therefore, the discussion will continue to focus on efficacy.

In the 1960's, Leander [47] published results of a carefully controlled trial. He compared placebo

with Cernitin pollen extract in 179 cases. Using pollen extract, Leander found a 60-80 per cent improvement over placebo in symptoms of obstruction, probably through elimination of inflammatory edema. Around the same time, much work was progressing in Japan. Inada et al [48] reported favorable effects in 12 patients suffering from prostatic hypertrophy. They reported that five cases had "effective" results; five showed "slightly effective" results and two reported "ineffective" results. In 1967, Ohkoshi, Kawamura and Nagakubo of Keio University, reported impressive results in 30 patients with prostatitis and/or urethritis [49]. Examining 14 patients receiving Cernitin, it was found that treatment was "successful" in 10, "slightly effective" in three, and "ineffective" in only one case. In 16 patients given placebo, seven found the treatment to be "effective" and nine reported "no change."

In 1981, Takeuchi [50] investigated both subjective and objective effects of Cernitin on 25 men with BPH. The efficiency rate for Cernitin was reported as 64%. There was a 50% improvement for nocturnal micturition. Horii et al [51] reported the results of 30 subjects with BPH who were given Cernitin 2 tablets, 3 times daily for at least 12 weeks. The overall clinical efficacy for subjective symptoms was rated at 80% and objective symptoms at 43%. Ueda et al [52] treated 22 patients with stage I and II BPH with Cernitin for over 4 weeks. Eighty-two percent of the patients were rated as moderately improved or better. Hayashi et al [53] treated 20 BPH patients with Cernitin, 6 tablets a day for an average of 13.2 weeks. They reported improvements in sense of residual urine (92%), retardation (86%), night frequency (85%), strain on urination (56%), protraction (53%), and forceless urinary stream (53%). Overall subjective effectiveness was 80% and overall objective effectiveness was 54%.

In 1986, a field study of 2,289 patients being treated by 170 urologists was undertaken [54]. They examined the effectiveness of Cernitin pollen extracts on chronic prostatitis and/or BPH. Improvement of symptoms was reported in 64 to 82%, in contrast to a low rate of adverse reaction found only in 2.9% of cases. In the same year [55], Brauer 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 flower pollen extract proved superior to beta-sitosterol in many respects, the mean values for residual volume fell under 15 ml for both at the end of treatment. Jodai et al [56] reported the results of a study on 32 patients with chronic prostatitis given 6 tablets of Cernitin daily for an average of 12 weeks. Subjective symptoms improved in 74.2% of the subjects as compared to 65.6% for objective symptoms. The overall efficacy rate was 75.0%.

In a double-blind, placebo-controlled study, Becker et al [57] reported data for 96 subjects with BPH in stages II or III according to the Vahlensieck. Subjects received two Cernitin capsules or placebo three times daily for 12 weeks. The results showed significant improvement in nocturia (68.8% on Cernitin versus 37.2% on placebo, $p = 0.005$), daytime frequency (65.8% on Cernitin versus 43.9% on placebo, $p = 0.076$), freedom from daytime frequency (48.8% on Cernitin versus 19.5% on placebo, $p = 0.010$) and freedom from sensation of residual urine (37.1% on Cernitin versus 7.7% on placebo, $p = 0.016$). In addition there was significant improvement in global assessment scores of both the physicians ($p = 0.001$) and patients ($p = 0.01$). Physicians rated the overall response as very good or good for 68.1% of patients taking Cernitin versus 13.7% taking placebo group. 72.1% of patients taking Cernitin rated their overall response as very good or good versus 27.3% in the placebo group. However, there was no significant change in the size of the prostate as determined by palpation.

In an open study, Buck et al [58] studied the effect Cernitin, 2 tablets twice daily for up to 18 months on 15 patients with chronic, relapsing non-bacterial prostatitis and prostadynia. Seven patients became symptom-free, 6 patients were significantly improved, and 2 patients failed to show improvement in symptoms. Improvement in symptomatology occurred for most patients after 3 months of treatment.

In a double-blind, placebo-controlled study, Buck et al [59] reported data for 53 subjects awaiting operative treatment for outflow obstruction due to prostate enlargement. Patients were instructed to take 2 capsules of Cernitin or placebo twice a day over a 6-month period. The results showed 60% of the subjects receiving Cernitin had less nocturia compared to 30% receiving placebo ($p < 0.063$), and 57% showed improvement in bladder emptying with Cernitin compared to only 10% taking placebo ($p < 0.004$). There was a significant difference ($p < 0.009$) in overall

improvement in subjective symptoms in the Cernitin group (69%) versus placebo (29%). Despite no significant change in peak urinary flow rate or voided volume, residual urinary volume decreased significantly in the Cernitin group compared to placebo ($p < 0.025$).

In a double-blinded, active-control study, Maekawa et al [60] conducted a double-blind study comparing Cernitin, 2 capsules twice daily for 12 weeks, to Paraprost (a mixture of the amino acids L-glutamic acid, L-alanine, glycine) in 159 patients with BPH. The two botanical preparations were comparable in improving symptoms (IPSS) from baseline (55% for Cernitin and 62% for Paraprost). There was a significant improvement in residual urinary volume, average flow rate, maximum flow rate and prostatic weight in the Cernitin group versus Paraprost. Greater than moderate effectiveness rating was 49.1% for Cernitin and 41.2% for Paraprost.

Becker et al [61] continued the placebo-controlled study described above [57] with an open label study in which 92 subjects previously treated in the first phase of the study with Cernitin (n=45) or placebo (n=47) were continued or now treated with Cernitin for 12 weeks. Physicians were blinded in this second phase as to whether the subjects received Cernitin or placebo in the first phase. The results showed that the differences observed between the two groups in the first phase were eliminated in the 2nd phase. Subjects previously treated with placebo improved significantly when treated with Cernitin. Significant improvements were observed in nocturia ($p = 0.051$), frequency ($p = 0.039$), feeling of incomplete emptying ($p = 0.013$), palpable enlargement of the prostate ($p = 0.046$) and prostatic congestion ($p=0.03$).

Bach and Ebeling [62] reported the results from a large open-label trial in Germany involving 208 physicians and 1798 patients with BPH capable of being evaluated. The patients were treated for 24 weeks with Cernitin; 2 tablets 3 times daily. The patients were divided into 3 groups (stage 1, 2 and 3) for data analysis based on the severity of the BPH symptoms. Patients in stage 1 had the most improvement of the three groups in irritative symptoms whereas patients in stage 2 had significant improvement in both irritative and obstructive symptoms. Peak urinary flow rates increased significantly in all 3 groups. A continuing improvement in symptoms was noted when comparing the results after 12 and 24 weeks of treatment. Efficacy in stage 1 and 2 patients was judged to be satisfactory or better in 90% of the patients. Efficacy in stage 3 patients was judged to be satisfactory or better in 65% of the patients. The authors concluded that treatment with Cernitin is justified even for stage 3 patients until surgery is performed.

Rugendorff et al [63] reported the results of a study on 90 patients with non-bacterial prostadynia and chronic prostatitis. Subjects were given Cernitin, 1 tablet 3 times daily for 6 months. Seven-two patients were found to have complicating factors (such as bladder neck sclerosis, prostatic calculi or urethral stricture), while the remaining 18 possessed no complicating factors. Seventy-eight percent of the patients without complications responded to the treatment with 36% of these becoming asymptomatic. In contrast, only 6% of patients with complicating factors improved. Peak urine flow rate in the uncomplicated group increased significantly ($p < 0.001$) from 15.9 to 23.5 ml/s.

Braun and Peyer [64] 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 patient receiving verum compared to 19 receiving placebo, there was a significant reduction in the mean number of both diurnal and nocturnal micturations 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.

Yasumoto and colleagues [65] conducted an open-label trial with 79 BPH patients. Patients were given 2 Cernitin tablets 3 times a day for at least 12 weeks. The results showed that symptom scores improved significantly from baseline. Overall clinical efficacy was rated 85%. Clinical efficacy at 12 weeks was rated satisfactory or better in 85% of the patients. Dutkiewicz [66] gave Cernitin to 51 patients with BPH -- 2 capsules three times daily for 2 weeks then 1 capsule 3 times daily for an additional 14 weeks. Thirty-eight subjects were given Tadenan (Pygeum africanum extract) for 4 months. Significant improvement in subjective symptoms was reported for both -- Cernitin group (78%) and the Tadenan group (55%). In a recently published

study, 24 patients with chronic prostatitis (NIH-category III) were treated with Cernitin for at least 6 weeks. The results showed a significant decrease in the symptom scores at 4 and 6 weeks [67].

Potential Role of Combination Therapy

Although published clinical trials support the efficacy of Cernitin in the relief of mild to moderate LUTS, a precedent exists to examine beneficial effects of combining Cernitin with other botanical products. A recently completed clinical study sponsored by the National Institutes of Health concluded that the combination of finasteride and doxazosin was more effective that either treatment alone in preventing progression of BPH [68]. This study demonstrates the therapeutic advantages of combining drugs with different mechanisms of action.

The precise mechanisms behind the therapeutic benefits of Cernitin are not fully understood, but it is generally accepted that anti-inflammatory and/or alpha adrenergic blocking effects are important. Therefore, combining Cernitin with a botanical and/or prescription drug with different mechanisms of action may provide additional symptomatic relief. Two recently published trials using combinations of agents with Cernitin support this theory.

Preuss et al [69] reported on a double-blind, placebo-controlled trial comparing a combination of Cernitin (378 mg); saw palmetto fruit standardized to 43% B-sitosterol (286mg) and vitamin E (100IU). Seventy subjects completed the combination therapy and 57 subjects completed the placebo over a 90-day period. There was a significant reduction in nocturia ($p < 0.001$), daytime frequency ($p < 0.04$) and overall symptomatology as measured by the American Urological Association Symptom Score. This combination therapy is logical, since saw palmetto may have different mechanisms of action than Cernitin. As an example, it is believed that saw palmetto compared to Cernitin prevents to a greater extent the conversion of testosterone to dihydroxytestoterone, a potent androgen that stimulates enlargement of the prostate [17,21,22].

Aoki et al [70] conducted an open label trial to study tamsulosin hydrochloride (Flomax®), an alpha1A adrenoceptor antagonist, Cernitin, and the combination in 243 patients with symptomatic BPH over a 12-week period. The results showed that whereas symptoms improved in each group, supporting the efficacy of Cernitin, the best results were obtained in the group that used the combination.

Discussion

A review of placebo-controlled trials, active-controlled and open-label studies indicate that Cernitin is a safe and effective therapy for the management of mild to moderate LUTS. By reducing bothersome symptoms, Cernitin improves quality of life. The placebo-controlled, double-blind studies with Cernitin alone [47,57,59,60] and combined with other natural products [69] especially provide evidence that Cernitin is effective in reducing nocturia, daytime frequency, and sensation of residual urine. The number of subjects in these studies was small relative to the studies conducted for prescription therapeutics such as Terazosin [11] (Hytrin, minimum of 430 subjects) and Doxazosin [71] (Cardura, minimum of 900 subjects), however the duration of the studies were comparable. Cernitin studies were generally conducted for 12 to 24 weeks, terazosin trials were conducted for 12 to 24 weeks, and doxazosin studies were also conducted over a 14 to 16 week period.

Since the number of subjects studied in placebo-controlled trials is small, it was necessary to review open-label and active control studies as supporting data. Concerning the use of Cernitin alone, we report on 15 open label studies and 4 double-blind, placebo-controlled studies that showed consistent reduction in subjective symptoms and overall effectiveness ratings of 75% and greater. In addition, 1 double-blind, active-controlled study, 1 open-label study on a combination, and 1 double-blind, placebo-controlled study on a combination strengthen the conclusions on the therapeutic merits of Cernitin.

Conclusions

Sufficient evidence exists in the primary and secondary literature to indicate that a standardized flower pollen extract commonly referred to as Cernitin is safe and effective for the treatment of mild to moderate LUTS. This dietary supplement composed of pollen extracts from rye, corn, and timothy has the potential to be used in combination with other dietary supplements or pharmaceuticals to provide relief of bothersome symptoms and improve quality of life for millions of men.

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