Efficacy of *Prunus africana, Urtica dioica* and *Epilobium angustifolium* in patients with benign prostatic hyperplasia

UMBERTO PANE[1], RAFFAELE GALASSO[2], RAFFAELE BAIO[1], OLIVIER INTILLA[1], UMBERTO DI MAURO[1] and ROBERTO SANSEVERINO[1]

[1]Department of Urology, Umberto I Hospital, Nocera Inferiore, I-84014 Salerno, Italy;
[2]Department of Urology, Maria SS. Addolorata Hospital, Eboli, I-84025 Salerno, Italy

Received May 3, 2024; Accepted October 18, 2024

DOI: 10.3892/ijfn.2024.42

Abstract. Benign prostatic hyperplasia (BPH) is a prevalent condition affecting aging males, causing lower urinary tract symptoms (LUTS) that affect the quality of life of patients. The present study aimed to assess the efficacy and safety of a combination of *Prunus africana, Urtica dioica* and *Epilobium angustifolium* extracts (Progamet), in conjunction with standard alpha blocker therapy, for the management of symptoms of BPH. The present study was an observational, controlled mono-centric trial including 92 male patients clinically diagnosed with BPH. The treatment group (n=46) received Progamet and alpha blockers for 90 days, while the control group (n=46) received alpha blockers alone. The primary endpoint was a change in the International Prostate Symptom Score (IPSS) after a period of 3 months. Secondary endpoints included urinary flow (Q-max), erectile function assessed using the International Index of Erectile Function (IIEF) score and safety. The treatment group exhibited a significant reduction in IPSS compared with the control group. The results of the present study also demonstrated that the Q-max was significantly increased in the treatment group, and there was a significant improvement in erectile function based on the IIEF score. Progamet was well-tolerated, with mild gastrointestinal side-effects reported in a small number of patients. On the whole, the results of the present study highlight the potential of Progamet as an alternative or complementary treatment for BPH. Herein, the combination of natural extracts, when administered alongside standard alpha blocker therapy, led to improved LUTS, urinary flow and erectile function. Thus, Progamet may exhibit potential for use in the management of BPH, providing symptomatic relief with minimal side-effects.

Correspondence to: Dr Raffaele Baio, Department of Urology, Umberto I Hospital, Alfonso De Nicola Street, Nocera Inferiore, I-84014 Salerno, Italy
E-mail: dott.rbaio@gmail.com

Key words: benign prostatic hyperplasia, lower urinary tract symptoms, quality of life, alpha blocker therapy, International Prostate Symptom Score

Introduction

Benign prostatic hyperplasia (BPH), also known as benign prostatic hypertrophy or benign prostatic obstruction, is a common condition affecting aging males. It involves the non-cancerous enlargement of the prostate gland, leading to lower urinary tract symptoms (LUTS) that may affect the quality of life of patients (1). The enlarged prostate presses against and pinches the urethra, causing the bladder wall to thicken. As a result, the bladder may weaken over time, leading to incomplete bladder emptying and urine retention (1). These changes in the urinary tract cause LUTS associated with BPH, such as urinary frequency (pollakiuria), urinary urgency, a weak urine stream and an increased need to urinate at night (nocturia) (2). At present, the specific cause of BPH is not yet fully understood. Changes in hormonal levels, particularly a decrease in active testosterone and an increase in estrogen levels, have been proposed as possible contributors to the development of BPH (3).

The results of a previous study suggested that dihydrotestosterone (DHT) may play a role in promoting prostate cell growth, even when testosterone levels are low (3). Inflammation and oxidative stress have also been proposed as potential contributors to the development of BPH (4). BPH is the most common condition of the prostate in males aged >50 years, and the prevalence of the disease increases with age. While <50% of males with BPH experience LUTS, the condition may lead to complications, such as acute or chronic urinary retention, blood in the urine, urinary tract infections, bladder and kidney damage, and bladder stones (5). At present, the pharmacological treatment of BPH involves medications that aim to reduce prostate growth or improve urinary symptoms. These medications include alpha blockers, phosphodiesterase-5 inhibitors, 5-alpha reductase inhibitors and combination therapies (2). Alpha blockers relax the smooth muscles of the prostate and bladder neck to improve urinary flow, while 5-alpha reductase inhibitors block the production of DHT, which may lead to shrinkage of the prostate or prevention of further growth. The aforementioned medications provide relief of the urinary symptoms associated with BPH; however, their use may lead to side-effects, including retrograde ejaculation, excessive reduction in blood pressure (orthostatic hypotension) and a reduced libido (6).

Research has focused on the use of alternative and complementary therapies for the management of BPH, including natural extracts derived from medicinal plants (7). This has led to the formulation of a combination of three specific plant extracts; namely, *Prunus africana, Urtica dioica* and *Epilobium angustifolium*. Traditionally, these individual plant extracts have been used for the treatment of urinary disorders. Thus, *Prunus africana, Urtica dioica* and *Epilobium angustifolium* may exhibit potential for use in the management of BPH. *Prunus Africana* (*Pygeum africanum Hook f.,* or *Prunus Africana Kalk.*), derived from the bark of the African plum tree, is used in traditional African medicine to alleviate urinary symptoms associated with BPH (8). The bioactive compounds, including phytosterols, triterpenes and ferulic acid esters, exhibit anti-inflammatory and anti-androgenic properties that may reduce prostate enlargement and improve urinary flow dynamics (8).

Clinical studies have demonstrated the efficacy of *Pygeum* extracts in reducing nocturia, improving the quality of life of patients and reducing International Prostate Symptom Score (IPSS) (9,10). *Urtica dioica* (*Urtica dioica L.* and/or *Urtica urens L.*), also known as stinging nettle root, is well-established in herbal medicine (11). Notably, *Urtica dioica* contains bioactive compounds, such as phytosterols (β-sitosterol, daucosterol and associated glucosides) and scopoletin. This extract also contains tannins, lecithins, mineral salts, phenylpropanes and lignans (11). Extracts derived from *Urtica dioica* exhibit anti-inflammatory and 5-alpha reductase inhibitory properties, which may improve hormonal symptoms associated with BPH. The results of clinical studies have demonstrated that extracts of *Urtica dioica* significantly improved LUTS, and these results were observed following short-term treatment (12,13). *Epilobium angustifolium* (*Onagraceae*), commonly known as small-flowered willowherb, is a plant used in traditional European medicine (14). *Epilobium angustifolium* contains flavonoids, tannins and phenolic acids that exhibit antioxidant and anti-proliferative properties, which may contribute to the alleviation of BPH (15). Enotein B, a main constituent of *Epilobium angustifolium*, has demonstrated immunomodulatory, antioxidant and anti-proliferative properties (16). It was thus hypothesized that a combination of the three plant extracts may exhibit potential as an alternative or complementary therapy for the management of BPH. Their respective bioactive compounds may exert synergistic anti-inflammatory, anti-androgenic and antioxidant effects, for the improvement of urinary symptoms and overall prostate health.

At present, research focused on the safety and efficacy of the combination of *Prunus africana, Urtica dioica* and *Epilobium angustifolium* is limited. Thus, the present study aimed to determine the effects of this herbal combination in patients diagnosed with BPH.

Materials and methods

Study design. The present study was an observational, controlled, mono-centric trial aimed at evaluating the efficacy of a combination of natural extracts (Progamet; USP-Union of Pharmaceutical Sciences S.r.l.; https://www.usponline.it/catalogo-prodotti/) derived from *Prunus africana*, *Urtica dioica* and *Epilobium angustifolium,* in addition to standard therapy (alpha blockers), for the treatment of symptoms associated with BPH. The present study aimed to assess whether the combination of these plant-based extracts improves the efficacy of the standard monotherapy in male patients diagnosed with clinical BPH, who were at an increased risk of clinical progression. The patients included in the present study were >50 years of age. The included patients presented with moderate-to-severe symptoms, an enlarged prostate (>30 cc) and prostate specific antigen (PSA) levels ≤1.5 ng/ml. All patients had visited the Department of Urology, Umberto I Hospital, Salerno, Italy. The present study was conducted following the Declaration of Helsinki, and was approved by the Campania SUD Ethics Committee (ethics approval no. 0152029). All patients provided written informed consent, and were divided into two groups as follows: i) The treatment group and ii) the control group. The patients in the treatment group received a daily dose of the natural extract combination in addition to the standard pharmacological therapy for 90 days. The control group received the standard therapy alone. Standard therapy had been prescribed to the patients before the commencement of the study and consisted in the use of alpha blockers, namely tamsulosin at 0.4 mg once daily, alfuzosin at 10 mg once daily and doxazosin at 4 mg once daily. Patients were consistently maintained on the same alpha blocker throughout the whole study period. All patients attended a screening visit (visit 1) and a baseline visit (visit 2). The patients included in the study presented with a total IPSS of ≥12 at visits 1 and 2. Following these initial visits, follow-up visits were scheduled 90 days after the baseline visit.

Patients were excluded from the present study according to the following criteria: i) Moderate or severe renal impairment, measured as creatinine clearance <50 ml/min, as estimated by the Cockcroft Gault formula; ii) severe hepatic impairment; iii) the concurrent use of other herbal or natural products that exert effects on LUTS (for example, *Serenoa serrulata/repens*); iv) a previous diagnosis of prostate cancer; v) an active urinary tract infection; vi) acute or recurrent prostatitis (>3 episodes over the past year); vii) a history of neurological disease that may influence bladder function; viii) a history of substance abuse, including alcohol or drugs over the past 12 months; ix) participation in a study involving the administration of an investigational compound over the past 30 days; and x) any other condition that, in the investigator's assessment, increased patient's risk, impeded optimal participation in achieving the study objectives, or highlighted that the patient was unable to complete the study.

Clinical investigation endpoints. The primary endpoint of the present study was a change in IPSS following 3 months of treatment, compared with the baseline. Secondary endpoints included the percentage of patients with an improved IPSS, an increase in maximum urinary flow rate (Q-max) from baseline, the percentage of patients able to reduce or discontinue standard pharmacological therapy, and a change in the International Index of Erectile Function (IIEF) score from baseline. The safety endpoint focused on monitoring any adverse events or complications associated with the use of the herbal extracts, as reported by patients.

IPSS. IPSS is a seven-item tool designed to quantify urinary symptoms in patients with BPH, with an additional eighth question regarding quality of life (17). IPSS was scored at Visit 1, Visit 2 and at the follow-up visit. The participants were instructed to refrain from using any alpha-adrenergic agonists, cholinergic or anticholinergic agents, including antihistamines or decongestants, within 48 h prior to each IPSS assessment. In addition, the patients were recommended to stop the use of selective beta-3-adrenoceptor agonists (mirabegron) for the treatment of overactive bladder syndrome 2 weeks prior to evaluation. Patients completed questionnaires as per the study schedule. The patients were instructed to complete the questionnaires in a quiet environment, in the same location each time, and consistently during study visits. Patients were encouraged to complete questionnaires in a thorough and accurate manner, without being influenced by test results or other external factors.

Prostate volume measurement. Prostate volume was measured at visit 2 (baseline) and after 90 days of treatment. The anteroposterior, cranio-caudal and transverse diameters of the prostate were obtained through suprapubic and/or transrectal ultrasound, to calculate prostate volume using the following formula: π/6 (anteroposterior width x cranio-caudal width x transverse width). Prostate volume measured with pre-programmed equipment was accepted if all three dimensions were emitted and recorded in the electronic case report form.

Urinary flow measurement. Urinary flow measurements were conducted using a uroflowmeter (Laborie Medical Technologies Corporation) at visits 1 and 2, and the follow-up visit. Maximal urinary flow (Q-max) with a voided volume ≥125 ml and residual urinary volume were recorded. The results are expressed as ml/sec (standard deviation; SD).

IIEF questionnaire. The IIEF questionnaire is a widely-used and validated self-administered tool designed to assess the presence and severity of erectile dysfunction in males (18). This questionnaire consists of five items that cover five domains associated with erectile function. Each item is scored on a five-point Likert scale, with responses ranging from 0 to 5. The total IIEF score was calculated following the addition of the scores of all five items, resulting in a score range of 0 to 25. Higher scores indicated improved erectile function and sexual satisfaction.

Clinical patient information, ECG and physical examination. The detailed medical histories of all patients were obtained at visit 1, including information on LUTS onset, time since BPH diagnosis, previous use of alpha-1-adrenoreceptor antagonists and/or herbal therapies, overall health, previous or current medical conditions, medication use, allergies, family history of cardiovascular diseases and sexual activity/sexual dysfunction. ECG and a complete physical examination were performed at visit 2.

Extracts. Natural extracts derived from *Pygeum africanum*, *Urtica dioica* and *Epilobium angustifolium* were contained in a supplement known by its commercial name, Progamet (USP-Union of Pharmaceutical Sciences S.r.l.; https://www.usponline.it/catalogo-prodotti/). Progamet was administered once daily the to patients in the treatment group, in addition to the standard pharmacological therapy for a duration of 90 days. Details regarding the standardized formulation and dosage were provided to the study participants in the form of an informational leaflet. The composition of Progamet includes the following standardized extracts: *Epilobium angustifolium L.* (Willowherb) standardized to 15% Oenothein B (600 mg), *Urtica dioica L.* (Nettle root) standardized to 0.8% Sterols (300 mg) and *Prunus africana* (Hook. f.) Kalkman (Pygeum bark) standardized to 2.5% beta-sitosterols (100 mg).

Statistical analysis. Sample size was calculated based on the estimated improvement in IPSS compared with the control, using information obtained from the CombAT study (19). Sample size estimates were made considering a continuous response variable with a normal distribution. The expected change in IPSS (mean difference between treatment groups) was estimated at 3.5 (SD, 6). With 80% power, the minimum required sample size per arm was calculated to be 46 subjects. Statistical analysis was performed using a independent sample two-tailed Student t-test, to determine whether the combination treatment was superior to standard therapy after 90 days. For the within-group analysis a paired sample two-tailed Student's t-test was used. A value of $P<0.05$ was considered to indicate a statistically significant difference. Descriptive statistics were used to summarize baseline characteristics of the study population. Continuous variables are presented as the mean ± SD, while categorical variables are presented as frequencies and percentages. Secondary endpoints were analyzed using appropriate statistical methods.

Results

Patients. A total of 92 patients were enrolled in the present study, with 46 patients assigned to the treatment group and 46 patients assigned to the control group. There were no clinically meaningful differences in demographic or clinical baseline characteristics between groups (Table I). The patients in the treatment group had a mean age of 65.09 (±10.9) years, and the patients in the control group had a mean age of 66.2 (±12.4) years. There was no notable difference in the mean body mass index (BMI) between the treatment and control groups. Notably, the mean BMI was 25.1 (±3.3) in the treatment group, and 26.0 (±1.5) in the control group. The mean prostate volume at baseline was 50.5 (±17.7) cc in the treatment group, compared with 48.2 (±8.5) cc in the control group. In the treatment group (n=46), comorbidities, such as hypertension (n=8, 17.4%), diabetes mellitus (n=6, 13.0%) and dyslipidemia (n=4, 8.6%) were documented alongside BPH. Similarly, in the control group (n=46), hypertension (n=4, 8.7%), diabetes mellitus (n=3, 6.5%) and dyslipidemia (n=2, 4.3%) were observed as the most common comorbidities. In the treatment group, 12 patients (26.0%) had prostates with characteristics of congestion, and 8 patients (17.4%) had prostates with inflammation (acute, subacute, or chronic).

Table I. Comparison of baseline characteristics and comorbidities between the treatment and control groups.

Parameters	Control	Treatment
Age, years (±SD)	66.2 (±12.4)	65.09 (±10.9)
BMI (±SD)	26.0 (±1.5)	25.1 (±3.3)
Prostate volume, cc (±SD)	48.2 (±8.5)	50.5 (±17.7)
Comorbidities	Hypertension (n=4, 8.7%), diabetes mellitus (n=3, 6.5%), dyslipidemia (n=2, 4.3%)	Hypertension (n=8, 17.4%), diabetes mellitus (n=6, 13.0%), dyslipidemia (n=4, 8.6%)
BHP presentation	Congestion (n=7, 15.2%) Inflammation (n=6, 13.0%)	Congestion (n=12, 26.0%) Inflammation (n=8, 17.4%)

SD, standard deviation; cc, cubic centimeters; BMI, body mass index.

Table II. IPSS scores in the control and treatment groups.

	Control group	Treatment group
Baseline IPSS	16.3 (±3.3)	19 (±3.3)
Follow-up IPSS	17 (±3.2)	14 (±3.7)
Change (Δ IPSS)	+0.7 (±3.2)	-5 (±3.7)
P-value	NS	<0.0001[a]
Between-group comparison P-value		<0.0001[a]

[a]Indicates statistically significant difference (P<0.05). IPSS, International Prostate Symptom Score; NS, not significant.

Table III. Comparison of urinary flow (Q-max) between the treatment and control groups.

	Control group	Treatment group
Baseline (SD)	14 (±2.7)	13 (±2.4)
Follow-up (SD)	14 (±2.1)	16 (±3.8)
Change (Δ Q-max)	0 (±2.0)	+3 (±2.6)
P-value	NS	<0.0001[a]
Between-group comparison P-value		<0.05[a]

[a]Indicates statistically significant difference (P<0.05). NS, not significant.

These observations indicate a heterogeneous presentation of BPH, similarly to the control group, where 7 patients (15.2%) had prostates with characters of congestion, while 6 patients (13.0%) had prostates showing signs of inflammation.

IPSS. IPSS was utilized as a primary outcome measure to assess the efficacy of Progamet in the management of LUTS associated with BPH. The results obtained are presented in Table II. In the treatment group, the mean baseline IPSS was 19 (±3.3). Following 90 days of Progamet supplementation, the follow-up IPSS was significantly decreased to 14 (±3.7; Table II and Fig. 1). Notably, the baseline IPSS in the control group was 16.3 (±3.3), and there was no significant change in follow-up IPSS (17±3.2; Table II; Fig. 1). The comparison of IPSS at follow-up demonstrated a notable difference in treatment efficacy. Thus, treatment with Progamet led to a clinically and statistically significant improvement in LUTS in the treatment group, compared with the control group. Collectively, these results demonstrated that treatment with Progamet led to a significant reduction in IPSS and improvements in LUTS in the treatment group, compared with the control group. The difference in treatment efficacy between the two groups was statistically significant.

Urinary flow measurement. The results of urinary flow measurement are presented in Table III. In the treatment group, the mean Q-max at baseline was 13 ml/sec (±2.4; Table III and Fig. 2). Following 90 days of treatment with Progamet, mean Q-max significantly increased to 16 ml/s (±3.8), indicating a statistically significant improvement in urinary flow (Table III and Fig. 2). In the control group, the mean Q-max at baseline was 14 ml/sec (±2.7), and this remained stable for 90 days [mean Q-max, 14 ml/sec (±2.1)]. These results highlighted that there was no significant change in mean Q-max (Table III and Fig. 2). Between-group comparisons revealed that following 90 days of treatment, the mean urinary flow was significantly higher in the treatment group [16 ml/sec (±3.8); Table III] compared with the control group (14 ml/sec ±2.1). Collectively, these results highlighted that 90 days of Progamet treatment led to a significant improvement in urinary flow. In addition, Progamet supplementation resulted in a significant increase in Q-max in the treatment group (ΔQ-max, +3 ml/sec), compared with no significant change in the control group (ΔQ-max, 0 ml/s). Notably, the difference in Q-max between treatment and control groups was statistically significant.

IIEF questionnaire. In the treatment group, the mean IIEF score at baseline was 15 (±5.5), indicating a moderate level of erectile function (Table IV; Fig. 3). At the 3-month follow-up, the mean IIEF score significantly increased to 16.5 (±5.6), indicative of an improvement in erectile function (Table IV; Fig. 3). In the control group, the mean IIEF score at baseline was 15 (±6.3), which was comparable with the treatment group (Table IV; Fig. 3). At the 3-month follow-up, the mean IIEF

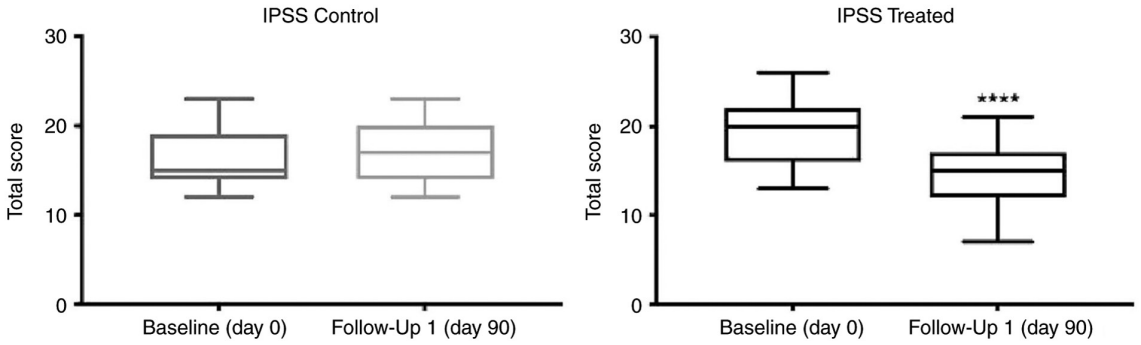

Figure 1. Comparison of IPSS between control and treatment groups at baseline (day 0) and follow-up (day 90). ****P<0.0001 vs. baseline. IPSS, International Prostate Symptom Score.

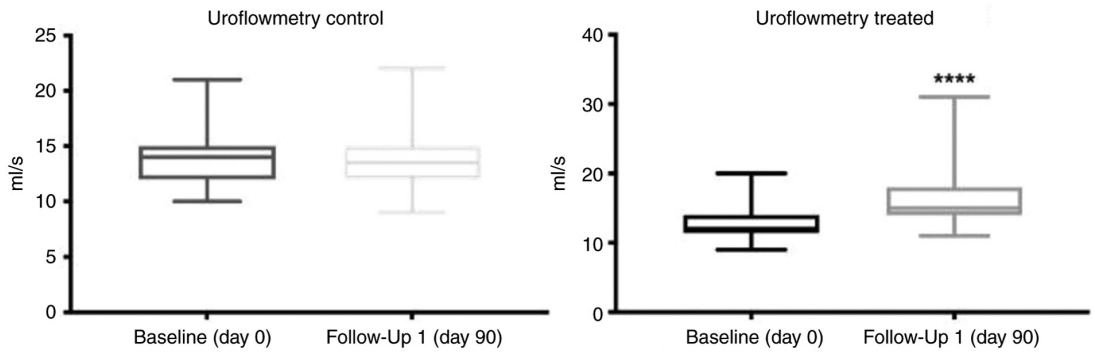

Figure 2. Comparison of urinal flow between control and treatment groups at baseline (day 0) and follow-up (day 90). ****P<0.0001 vs. baseline.

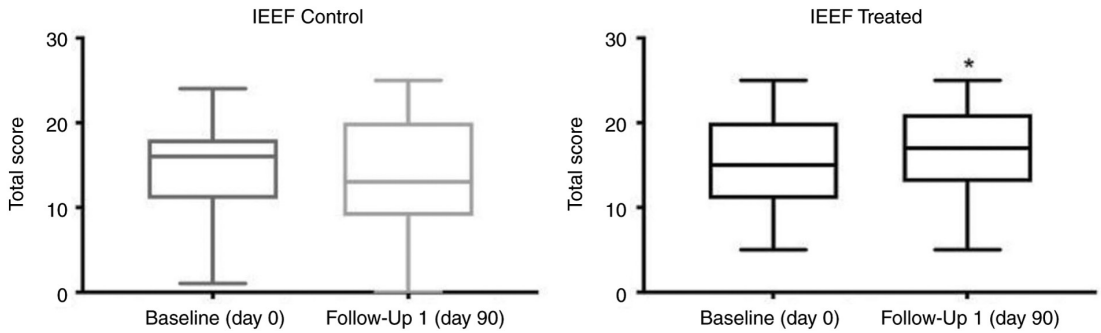

Figure 3. Comparison of the IIEF score between control and treatment groups at baseline (day 0) and follow-up (day 90). *P<0.05 vs. baseline. IIEF, International Index of Erectile Function.

score markedly decreased to 14 (±7), suggesting a minor decline in erectile function. However, this change was not statistically significant (Table IV; Fig. 3). When comparing the change in the IIEF score the between treatment and control groups, the observed improvement in erectile function in the treatment group was statistically significant (Table IV). Collectively, these findings suggested that treatment with Progamet exerted a positive impact on sexual function. In addition, a significant increase in IIEF score (ΔIIEF score, +1.5) was observed in the treatment group following 90 days of Progamet supplementation, indicating an improvement in erectile function. By contrast, a notable decrease in IIEF score (ΔIIEF score, -1) was observed in the control group, suggesting a minor decline in erectile function. However, this result was not statistically significant.

Percentage of patients able to reduce or discontinue standard pharmacological therapy. Patients responding well to treatment were instructed to reduce or discontinue the standard pharmacological treatment. Among these, 8 patients (17%) were able to discontinue the standard pharmacological treatment after ~2 months of using Progamet. After terminating the standard pharmacological treatment, patients did not report a worsening of symptoms. At follow-up, all patients demonstrated an improvement of all scores compared with baseline. Notably, no patients in the control group were able to discontinue the standard pharmacological treatment. Data were analyzed using the Chi-squared test, and the results demonstrated that the percentage of patients who discontinued the standard

Table IV. Comparison of the IIEF score between the treatment and control groups.

	Control group	Treatment group
Baseline IIEF Score	15 (±6.3)	15 (±5.5)
Follow-up IIEF Score	14 (±7)	16.5 (±5.6)
Change (Δ IIEF Score)	-1 (±1.5)	+1.5 (±1.5)
P-value	NS	<0.05[a]
Between-group comparison P-value		<0.05[a]

[a]Indicates statistically significant difference (P<0.05). NS, not significant; IIEF, International Index of Erectile Function.

Table V. Contingency table demonstrating the number of patients who discontinued the pharmacological treatment (Yes).

Data analyzed	Yes	No	Total
Progamet	8[a]	38	46
CTRL	0	46	46
Total	8	84	92

[a]P<0.05, indicating a statistically significant difference.

pharmacological treatment was statistically significant (P<0,05). (Table V).

Safety evaluation. Throughout the study period, patients responded well to treatment. Side-effects were observed in a small group of patients, and the most common side-effects included gastrointestinal problems, such as diarrhea and nausea. The safety profile of Progamet remained consistent and comparable across all study participants.

Discussion

Conventional pharmacological treatments offer symptomatic relief for BHP; however, such treatments may induce potential side-effects that are not well-tolerated by some patients (6). This has led to an increased interest in the use of natural alternatives, such as plant extracts, which may possess therapeutic properties that are beneficial for BHP. Herbal products are frequently administered to male patients in Western Europe who are experiencing LUTS (20). The results of a previous study demonstrated positive outcomes in patients with BPH, following treatment with a combination of extracts derived from *Urtica dioica* and *Prunus Africana* (9). Extracts derived from *Epilobium angustifolium* have also demonstrated favorable results in patients with BHP (15). Notably, *Epilobium angustifolium* contains enotein B, a polyphenol with immunomodulatory properties (21). The aforementioned results led to the formulation of Progamet, a combination of three specific plant extracts; namely, *Prunus africana*, *Urtica dioica* and *Epilobium angustifolium*. In the present study, significant improvements in IPSS were observed in the treatment group compared with the control group, and these results were indicative of reduced LUTS. An improvement in LUTS following 90 days of treatment highlighted the potential of Progamet as a complementary therapy to standard treatment with alpha blockers. In addition, patients in the treatment group demonstrated notable improvements in urinary flow.

An increase in urinary flow observed after 90 days of Progamet supplementation highlighted the potential of this treatment in reducing urinary obstruction resulting from prostate enlargement. Improvements in urinary dynamics observed in the present study are consistent with those observed following treatment with each individual plant extract, indicating a potential synergistic effect within the Progamet formulation (8,9,15). Sexual function, often adversely affected by BPH, was assessed using the IIEF questionnaire. The results of the present study revealed a statistically significant improvement in erectile function within the treatment group, which was not observed in the control group. This result suggested that Progamet supplementation may positively affect sexual function, offering additional benefits to patients with BPH. In addition, Progamet demonstrated a positive safety profile. Mild and transient gastrointestinal side-effects, such as diarrhea and nausea, were reported in a small group of patients in the treatment group. Such effects are consistent with those observed in previous studies involving the individual plant extracts, further verifying the overall safety of the formulation (9,10,12,13). In conclusion, the results of the present study highlighted the potential use of Progament in the management of symptoms in patients with BPH, including improved LUTS, urinary flow and erectile function.

While the mechanisms of action of the single phytotherapeutic agents are yet to be fully understood, the plant extracts in Progamet may function synergistically in the treatment of BHP. Each component of the exerts an effect that may be benefic to treat BPH. In particular, *Prunus africana* has been shown to inhibit the binding of DHT to androgen receptors in the prostate (22). Since DHT plays a key role in BPH, reducing its effect on the prostate helps in managing symptoms. *Urtica dioica* root is believed to bind to the sex hormone binding globulin, thereby reducing the amount of free testosterone converted into DHT, which is a major contributor to prostate enlargement (23). *Epilobium angustifolium* inhibits the enzyme 5-alpha-reductase and helps to protect prostate cells from oxidative stress and inflammation (24,25). The formulation used, by combining these three extracts, may likely function by reducing DHT levels in the prostate through the inhibition of 5-alpha-reductase, alleviating inflammation in prostate tissue, thereby reducing swelling and improving urinary function and supporting improved bladder contractility and relieving urinary retention symptoms often associated with BPH.

However, the present study exhibits limitations. Notably, the study duration was brief, with treatment being administered for 90 days. In addition, the present study had a moderate sample size and lacked a placebo group for further comparison.

Thus, further investigations with increased sample sizes are required, to determine the specific mechanisms of action and long-term safety profile of this treatment combination. Further investigations may provide a more comprehensive understanding of the potential benefits observed in patients with BPH following treatment with Progamet.

The results of the present study highlighted the potential of Progamet, a composite herbal formulation of *Prunus africana*, *Urtica dioica* and *Epilobium angustifolium* extracts, in addition to standard alpha blocker therapy, in addressing the symptomatic burden of BPH. Based on the safety profile of the treatment observed in the present study, this formulation may exhibit potential as an alternative or complementary treatment in patients with BPH. Notably, Progamet may provide patients with an alternative to conventional medications. As the population ages and the prevalence of BPH increases, further investigations into the use of natural remedies are required. The combination of plant extracts included in Progamet, each with established medicinal properties, may provide effective treatment for BPH. In conclusion, results of the present study demonstrated the efficacy of Progamet in patients with BPH. Notably, a diverse range of treatment options are available for patients, which may lead to improved quality of life and an increased choice of holistic healthcare approaches.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

UP, RG and RB made substantial contributions to the conception and design of the study. RS, UDM and OI interpreted the patient data. UP and RB confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

The present study was conducted following the Declaration of Helsinki, and was approved by the Campania SUD Ethics Committee (ethics approval no. 0152029). All patients provided written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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