

Monograph of Pygeum Africanum



[www.bodyandfitness.com/images/ Herbs/burdock1.jpg](http://www.bodyandfitness.com/images/Herbs/burdock1.jpg)

- I. **Herbal/Supplement Name**¹
 - a. African Plum Tree

- II. **Scientific/Common Names**¹
 - a. Prunus Africana
 - b. Pygeum Africanum

- III. **Family**^{1, 2}
 - a. Rosaceae

- IV. **Active Ingredients**^{1, 2}
 - a. The active ingredients are extracted from the bark of the herb
 - b. 14% triterpenes (urolic acids, oleanolic acid, crataegolic acid)
 - c. 0.5% n-docosanol
 - d. Phytosterol (β -sitosterol, β -sitosterone, Campesterol)

- V. **Mechanism Of Action**¹⁻⁵
 - a. Extracts have anti-proliferative effects on fibroblasts and inhibits bladder hyper-reactivity, which are over produced in BPH.
 - b. Phytosterols competes with androgen precursors and inhibit prostaglandin biosynthesis to reduce prostatic cholesterol levels.
 - c. Triterpenes have anti-inflammatory activity by inhibiting enzymes involved in the depolymerization of proteoglycans in prostate connective tissue.
 - d. Improves symptoms of BPH and prostatic adenoma (esp. nocturia, flow rate, voided volume, and/or residual volume) by increasing prostatic secretions and improves seminal fluid composition.

- VI. **Indications**^{1-4, 6, 7}
 - a. Common use
 - i. Benign prostatic hypertrophy (BPH) and prostatic adenoma (nocturia, dysuria, pollakiuria, micturitional disorders, and/or bladder fullness)
 - b. Other use:
 - i. Fertility disorder
 - ii. Urinary tract infections (UTI) (inflammation and/or difficult urination)
 - iii. Inflammation
 - iv. Kidney disease
 - v. Malaria
 - vi. Stomachache
 - vii. Fever
 - viii. Madness
 - ix. Aphrodisiac

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VII. **Efficacy**^{4, 6, 8, 9}

- a. Breza J, et al, performed an open-label uncontrolled study in patients suffering from mild to moderate benign prostatic hyperplasia (BPH) symptoms (urinary frequency (day and/or at night), urgency, straining in order to commence urination, weak urinary stream or dribbling, and/or sensation of incomplete emptying of bladder). Eligible patients were entered into the treatment phase: P. africanum extract, Tadenan[®], 50mg twice daily (AM & PM dosing) for two months.
 - i. Inclusion criteria included male patients aged 50 to 75 years old, mentally alert with good physical health, and with a diagnosed of moderate symptomatic BPH via questionnaire (micturitional problems \geq 6 months (e.g. nocturnal frequency), a score at the inclusion visit V1 of \geq 12 on the IPSS scale, and a QOL score at visit V1 of \geq 3 on the QOL scale of Mebust), digital rectal examination (prostatic hyperplasia characteristic of “adenomatous” lesion), uroflowmetry (max urinary flow rate \leq 15ml/s and voiding volume or urine volume \geq 150ml), transabdominal ultrasonography (residual urinary volume $<$ 100ml and prostate volume $<$ 100ml), and biochemical criteria (SrCr $<$ 160 μ mol/L, Serum prostate specific antigen (PSA) \leq 4ng/ml or PSA density $<$ 0.15, and urine bacterial count $<$ 10⁵/ml).
 - ii. Exclusion criteria included patients suffering from any disease or history of surgical intervention on the prostate or bladder, micturitional problems due to identified bladder pathology (e.g. neurogenic bladder, bladder neck stenosis, lithiasis, bladder cancer, etc), known urethral stricture, diagnosed prostatic cancer, recurrent urinary infections, BPH judged by investigator (urologist) to need surgical treatment, known renal, hepatic, or cardiac insufficiency, or hypersensitive to P. africanum extract. Plus, patients unable to understand or follow the study protocol or is/are involved in another clinical trial within the past 3 months.
 - iii. Methods, 85 patients from 3 different centers (Warsaw, Bratislava, and Prague) with an overall mean age of 63.35 \pm 6.28 years were evaluated at the first visit (V1), then a 2 weeks wash-out period without treatment (V2) to check for condition stability, thereafter patients were entered into the treatment phase: P. africanum extract, Tadenan[®], 50mg twice daily (AM & PM dosing) for two months (V3-1st month and V4-2nd month), plus reassessment after 1 month of completing the treatment phase (V5) (at this time patient is no longer on medication).

- iv. Primary outcome measured was the mean change in IPSS score (scale 0-35) from baseline visit V2 to V4 after 2 months of active treatment. Results showed, average total IPSS for all 3 centers at visit V1 = 16.29 ± 3.79 and visit V2 = 16.17 ± 3.38 . When the mean of V1 and V2 were compared this showed that during the 2 weeks washout period the patients' conditions were stable. At V3 IPSS was relatively reduced by 31% when compared to V2 and was 40% at V4 and V5 ($P < 0.001$).
- v. Secondary outcomes measured were changes from baseline of V2 to V4 for nocturnal urinary frequency (IPSS question 7), QOL, max urinary flow rate, average urinary flow rate, urinary volume, and changes in post-micturitional residual volume and prostatic volume. Results showed, QOL scores in all 3 centers were similar in terms of mean value at visit V1 = 3.66 ± 0.76 and at visit V2 = 3.60 ± 0.74 , the mean change after 2 weeks washout period was not statistically significant. However, QOL was statistically significant at V4 = 31% and V5 = 34% improvement from baseline ($P < 0.001$). Nocturia, according to the IPSS questionnaire the mean at visit V2 for all centers was around 2.6 times/night, the change between V1 and V2 lacked statistical significant. However, at V3 = 1.95 times/night and V4 = 1.66 times/night, the changes between V2 and V4 gave a 32% reduction ($P < 0.001$). At the beginning of the study, more than half of the patients getting up to urinate at night ≥ 3 times but by the end of the 2 months treatment phase (V4) it was reduced to 16 patients. The mean maximal urinary flow and average urinary flow increased from baseline at V3 (10.97 to 13.07ml/s and 5.94 to 6.93ml/s) and with additional improvement at V4 ($P < 0.001$). Urinary volume at V4 increased from baseline of 218.63ml to 264.04ml ($P < 0.01$). There was no statistically significant change in post-micturitional residual volume from baseline to V4 (32.60ml to 29.62ml).
- vi. Safety assessment, at each of the 5 visits investigator assessed biochemical and haematological safety by patient reports and conventional laboratory tests (differential blood count, platelets, creatinine, ASAT, ALAT, γ -GT, and alkaline phosphatase). In addition, at V2 and V4 patients were asked to complete a simplified sexual life questionnaire (e.g. improved, remained unchanged, or got worse). Results showed, at V2 = 89% (76/85) of patients were satisfied with their sexual life, of these patients 7 claimed improvement at V4. However, 3 patients went

from “satisfactory” to “got worse” at V4 and 1 patient had been impotent for several years remained impotent. Furthermore, no adverse events or clinically relevant changes in biochemical parameters were observed (there was 3 increased PSA in the Warsaw group but was not associated with the development of prostatic carcinoma).

vii. Conclusion, according to this study and others *P. africanum* is effective and safe under the open-label conditions because beneficial effects can be seen after one month of treatment with a tendency to further improved by the second month.

- b. Chatelain C, et al, preformed a randomized, parallel, double blind, with a long-term open label study comparing once daily dosing to twice daily dosing of pygeum africanum extract in patients with benign prostatic hyperplasia.
- i. Inclusion criteria included age ≥ 50 , showed clinical symptoms of BPH (urinary symptoms, International Prostate Symptom Score (IPSS) ≥ 10 , and quality of life (QOL) ≥ 3), prostate volume $\geq 30 \text{ cm}^3$ confirmed by digital rectal examination and transrectal ultrasound, voided volume $\geq 140\text{mL}$, residual volume $\leq 150\text{mL}$, prostate-specific antigen (PSA) $< 10\text{ng/mL}$, and SrCr $< 160\mu\text{mol/L}$.
 - ii. Exclusion criteria included candidates for or had previous prostate or bladder surgery, prostate and/or bladder cancer, urinary symptoms due to other causes, and treatment during the 3 months preceding inclusion with finasteride, *P. africanum*, *Serenoa repens*, or with any α -blocker during 1 month before inclusion.
 - iii. Primary outcome was to achieve $\geq 40\%$ reduction in the mean IPSS from baseline and the main efficacy end point was the % of patients reaching this goal.
 - iv. Secondary outcome measures were global IPSS, nocturia, QOL, voided volume, residual volume, and prostate volume. Safety was assessed on drug side effects, vital signs, clinical biology, serum PSA at 12 months, and satisfaction of the patients’ sexual function.
 - v. Methods, 101 patients were randomized to group A (50mg twice daily) and 108 patients to group B (100mg once daily) for duration of 2 months. In addition, the first 174 patients that completed the comparative phase were enrolled in the open-label extension phase (an additional 10 months of treatment with 100mg once daily regimen).
 - vi. Comparative phase results, for efficacy the % of patients achieving therapeutic goal for group A was 42.6% (95% CI 33% to 53%) and group B was 40.7% (95% CI 31% to

- 51%). IPSS decreased similarly in both groups. The mean IPSS was reduced from 17.2 (group A) and 16.7 (group B) to 10.7 (-37.6%) and 10.9 (-34.6%). Nocturia improved equally in both groups, from 2.3 to 1.5 in both groups. QOL improved in both groups, from 4.3 (group A) and 4.1 (group B) to 3.1 and 3.0. Voided volume increased by 1.63mL/s (16%) in group A and 2.02mL/s (18.6%) in group B. Residual volume did not vary significantly.
- vii. Open-label extension phase results, the % of patients reaching the therapeutic goal increased with time: 20.1% at 1 month, 42.0% at 2 months, 57.1% at 5 months, 65.4% at 8 months, and 62.8% at 12 months. The mean IPSS decreased from 16.2 (baseline) to 8.7 (-46.3%). Nocturia after 12 months decreased from 2.3 to 1.4. QOL improved from 4.1 (baseline) to 2.4 (-41.5%) and after 12 months 58.1% of patients had a score ≤ 2 . Prostate volume at the end of the study was reduced from 42.0 to 39.9 cm³. Voided volume and other urinary parameters improved after 2 months of the study and maintained improvement even after 12 months.
- viii. Safety assessment results, no significant changes in blood or urinalyses in either group or during the study. At 12 months there was no significant variation of the PSA level. After 2 months, sexual activity was not significantly affected. The most common side effects reported were gastrointestinal (constipation, dyspepsia, nausea), but most were not related to treatment. In the comparative phase, 2.6% of patients experienced drug related side effects and 2.9% in the open-label extended phase (refer to table IV). Furthermore, in the comparative phase 1.3% of patients experienced serious side effects (muscular and joint pain, dysuria, urinary retention, hematuria, meningeal carcinoma, and/or subdural hematoma) and 4.0% in the open-label extended phase. All together 23 patients dropped out from the study: 8 (4.6%) due to adverse events and 15 (8.6%) for non-medical reasons.
- ix. Conclusion, *P. africanum* is considered as an alternative treatment for patients with mild to moderate symptoms of BPH. The recommended regimen is with *P. africanum* extract 100mg daily or 50mg twice daily for 12 months are both safe and efficacious for the treatment of mild to moderate BPH. Currently there is no reporting or mentioning of the long-term effects (≥ 12 months) on efficacy or safety issues with the usage of this herb.

- c. Lucchetta G, et al, performed a study focused on men with reduced prostatic secretion in the ejaculate at 2 successive examinations. The thought is that *P. africanum* bark extract is known to stimulate prostatic secretion therefore can this extract increase the amount of prostatic secretion of a normal physiological composition which would enable the spermatozoa to mature under optimum conditions. The authors hypothesized that *P. africanum* extract's effects would be more apparent in cases where the initial reduction was greater.
- i. Methods, 22 males with reduced prostatic secretion combined with reduced fertility got their ejaculate analyzed as follows: 1) spermatozoa and round-cell count (million/cm³) 2) motility at 1 and 6 hours 3) % of 'normal' shaped cells 4) determination of volume and pH 5) determination of protein concentration (followed Lowry's method but modified by Eggstein) 6) determination of fructose (resorcinol technique) 7) determination of acid phosphatase activity (p-nitrophenyl phosphate technique) 8) detection of IgA by antiserum anti-IgA (produced by Behring, batch #1000834 with Ouchterlony technique). Patients were given two tablets of *P. africanum* to be taken three times daily for 3 months (no documentation of strength). At the end of treatment phase, 2 sperm counts will be collected and examined followed the treatment at 1week interval.
 - ii. Inclusion criteria included males from the sterility clinic with prostatic secretion insufficiency at 2 sperm counts carried out at 1week interval (prostatic phosphatase activity < 400IU/ml).
 - iii. No mention of exclusion criteria
 - iv. Results, the effects of treatment on semen parameters (number of round cells (million/cm³), % of motility at 1 hour, and fructose (g/l) showed no statistically significant when comparing the treatment. However, the semen parameters that showed statistically significant results were the number of spermatozoa (million/cm³) (P = 0.01), proteins (g/l) (P = 0.05), and acid phosphatase activity (IU/cm³) (P = 0.05) (Table 1). Effects of treatment on the various protein groups indicated a reduction in serous proteins. Quantitative analysis shows in 4 cases the prealbumins present before treatment completely disappeared after treatment (Table II). Treatment in patients with or without IgA in the seminal fluid showed that the presence of IgA in the seminal fluid causes a reduction in the efficiency of the treatment (P = 0.05) (Table III).

- v. Conclusion, *P. africanum* extract does produce an increase in prostatic secretion in patients with reduced fertility and diminished prostatic secretion. In patients without infectious state the increase was more significant, therefore improvement of seminal fluid composition should lead to a better maturation of spermatozoa.

VIII. **Contraindications & Allergies**^{2, 4}

- a. Pregnancy
- b. Lactation
- c. Children
- d. Hypersensitive to pygeum

IX. **Dosage forms**^{2, 4}

- a. Powder
- b. Capsule
- c. Tablet

X. **Recommended Doses & Duration**^{1-4, 6, 7}

- a. Orally take 100mg daily or 50mg twice daily (max dose of 200mg/day) of standardized lipophilic extract (unknown component partials), it is safe and effective for functional symptoms of BPH for 6-8 week cycles.
- b. Orally take 2 tablets three times a day for 3 months for fertility disorders (unknown strength).
- c. Currently there is insufficient reliable information available about the usage of pygeum for its other indications.

XI. **Drug Interaction and Drug-Disease Interactions**^{1, 2, 4}

- a. Unknown due to no reporting and/or lack of human data available.

XII. **Adverse Reactions/Side Effects**^{2, 4}

- a. GI: Nausea, vomiting, diarrhea, abdominal pain, anorexia, and/or irritation
- b. Skin: Hypersensitivity reactions

XIII. **Safety Issues**^{1-4, 6, 7}

- a. The safety and efficacy of pygeum extract has been demonstrated in numerous short-term (approximately 8 week duration) open label studies and several controlled studies in men to reduce fertility problems and diminish benign prostatic hyperplasia. However, no studies have been performed in pregnancy, lactating women, or children. Therefore, it is contraindicated in these populations due to unavailable or unreliable findings.

XIV. **Comments**²⁻⁴

- a. Pygeum is an evergreen found in southern and central Africa.
- b. Since 1969, France has been using *P. africanum* extract of the bark to treat symptomatic benign prostatic hyperplasia.
- c. The contraindicated population needs to avoid usage due to lack of safety evidence. If hypersensitivity reaction occurs then patient needs to discontinue using the drug and initiate antihistamine or other appropriate therapy to treat the reaction.
- d. Other herbals available for the treatment of BPH: Alfusosin, Saw Palmetto, or Gonadorelin.

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