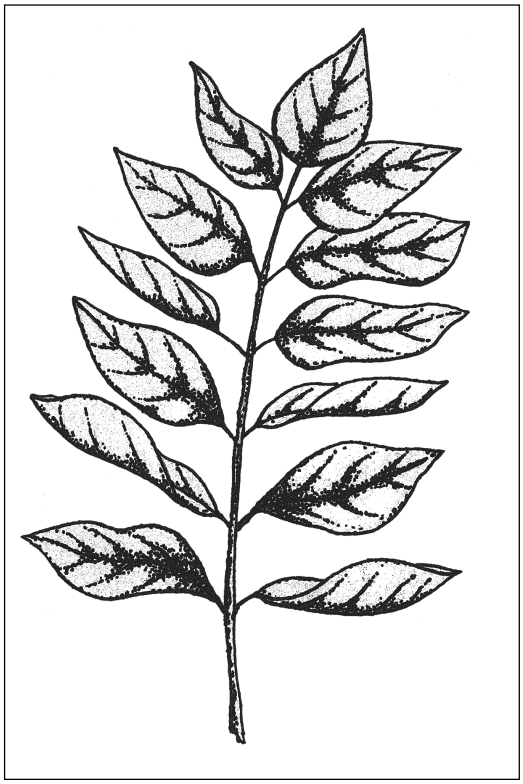
Pygeum africanum (*Prunus africana*) (African plum tree)

Introduction

Pygeum africanum, a member of the Rosaceae family, is an evergreen species found across the entire continent of Africa at altitudes of 3,000 feet or higher. It grows up to 150 feet tall. Interest in the species began in the 1700s when European travelers learned from South African tribes how to soothe bladder discomfort and treat "old man's disease" with the bark of *P. africanum*.[1] Pygeum bark extract has been used in Europe since the mid-1960s to treat men suffering from benign prostatic hyperplasia (BPH).[2] Currently, Pygeum is the most commonly used medicine in France for BPH, backed by many double-blind studies pointing to its efficacy for reducing its symptoms.[3, 4]



Active Constituents

The active constituents of Pygeum extract include phytosterols (e.g., beta-sitosterol) that have anti-inflammatory effects by inhibiting production of pro-inflammatory prostaglandins in the prostate. Pygeum also contains pentacyclic triterpenes (ursolic and oleanic acids) that have anti-edema properties, and ferulic acid nesters (n-docosanol and tetracosanol) that reduce prolactin levels and block the accumulation of cholesterol in the prostate. Prolactin is purported to increase the uptake of testosterone by the prostate, and cholesterol increases binding sites for dihydrotestosterone (DHT).[1,5]

Mechanisms of Action

Although Pygeum's exact mechanism of action is still unclear, in animal models Pygeum has been shown to modulate bladder contractility by reducing the sensitivity of the bladder to electrical stimulation, phenylephrine, adenosine triphosphate, and carbachol.[4] Pygeum also has anti-inflammatory activity, by decreasing production of leukotrienes and other 5-lipoxygenase metabolites (lower concentrations of Pygeum can be used to decrease 5-lipoxygenase metabolites when first dissolved in DSMO).[6] Furthermore, Pygeum inhibits fibroblast production, increases adrenal androgen secretion, and restores the secretory activity of prostate and bulbourethral epithelium.[4,7]

Basic fibroblast growth factor (bFGF) is hypothesized to play a role in the development of BPH and Pygeum has been shown to have a significant inhibitory effect on cell proliferation induced by bFGF.[7-9] Furthermore, in patients with abnormally low prostatic acid phosphatase activity, *P. africanum* extract can restore acid phosphatase activity and total protein secretion, although it is more effective in patients without prostatic inflammation.[10]

Clinical Indications

Benign Prostatic Hypertrophy

In one of the largest placebo-controlled, double-blind studies (n=263), Pygeum administered at a dosage of 100 mg per day for 60 days improved urinary maximum flow by 17.2 percent, increased voided volume by 12 percent, decreased residual volume by 24.5 percent, decreased nocturia by 31 percent, decreased daytime frequency by 19.4 percent, and resulted in overall improvement of 50 percent. Sixty-five percent of the subjects reported an improvement in this study as compared to 31 percent in the placebo group.[11]

A recent literature review analyzed studies from 1966-2000 containing a total of 18 randomized, controlled trials involving 1,562 men. The reviewers concluded that, compared with placebo, *P. africanum* provided a significant improvement in the combined outcome of urological symptoms and flow measures. In addition, subjects taking Pygeum extract were more than twice as likely to report an improvement in overall symptoms; nocturia was reduced by 19 percent and residual urine volume by 24 percent; and peak urine flow was increased by 23 percent.[3]

A lengthy 1995 literature review of the use of Pygeum extract for BPH also yielded positive findings for its efficacy. Twelve double-blind, placebo-controlled studies of *P. africanum* extract were analyzed in which 358 patients received *P. africanum* extract and 359 received placebo. Taken as a whole, the results show a statistically significant benefit for *P. africanum* extract over placebo. Unfortunately, most of the studies had small patient numbers, although one study with 126 subjects showed a statistically significant benefit for Pygeum extract in maximum urinary flow rate, voided volume, residual volume, nocturia, daytime frequency, and impression of improvement scored by physicians and patients.[4]

In an experiment with 209 subjects with BPH using a parallel-group, double-blind, comparative phase (group A, 50 mg twice daily; group B, 100 mg once daily) and a ten-month open phase (100 mg once daily), the average International Prostate Symptom Score (IPSS) improved by 38 percent in group A and 35 percent in group B. Furthermore, the quality of life (QOL) index improved 28 percent in both groups, and the maximum urinary flow rate (Qmax) increased 16 percent in group A and 19 percent in group B.[12] After 12 months, the IPSS decreased an average of 46 percent and the Qmax increased 15 percent. In another open phase trial testing the efficacy of Tadenan, a plant extract from Pygeum, 85 patients had significant improvements in IPSS (40%), QOL (32%), and nocturnal frequency (32%). Improvements in Qmax, average urinary flow, and urine volume were also statistically significant.[13]

In four relatively small studies, *P. africanum* was compared with: (1) sitosterin (n=53), (2) *Urticae urtae* radix extract (n=42), (3) non-steroidal anti-inflammatory or anti-infective treatment (n=39), or (4) non-steroidal anti-inflammatory treatment only (n=49). Although the results favored *P. africanum* extract over the other treatment groups, only a small number of patients were studied, and no statistical comparisons were made among treatments.[4]

Chronic Prostatitis

P. africanum extract (100 mg/d for 5-7 weeks) was used to treat 47 patients with chronic prostatitis (8 septic, 39 non-septic) in an open-label study. Eighty-nine percent of patients experienced complete remission of symptoms; whereas, there were no improvements in three septic patients and two non-septic patients.[4] In another study, *P. africanum* extract (200 mg/d for 60 days) was used either alone or in combination with antibiotics to treat 18 patients suffering from sexual disturbances due to either BPH or chronic prostatitis. Pygeum improved all the urinary parameters investigated

by medical history and prostatic transrectal echography, and improved sexual function despite the fact there were no significant differences found between hormonal levels and nocturnal penile tumescence and rigidity monitoring before and after therapy. The authors stated that the results should be confirmed by other investigators but suggested *P. africanum* extract may be beneficial in the treatment of patients with sexual/reproductive dysfunction.[14]

Obstruction-induced Contractile Dysfunction

The obstructive component of the enlarged prostate often results in bladder outlet obstruction (BOO) due to increased outlet resistance. BOO results in detrusor muscle hypertrophy, hyperplasia, and instability, as well as collagen deposition. Tadenan was tested in four groups of New Zealand white rabbits to determine its ability to protect the bladder from contractile dysfunction caused by experimentally-induced BOO. In this study, Tadenan had a significant outcome of reducing the effect of BOO on bladder mass and reversing the contractile response secondary to urethral obstruction. These improvements were associated with Pygeum's ability to alter the expression of myosin isoforms (the contractile proteins in muscle fibers).[15] A similar study also found Tadenan was able to reverse bladder dysfunction induced by mild BOO and improve bladder function with severe BOO.[16] Tadenan has also been proven effective protection when administered as a pretreatment to rabbits prior to experimentally-induced BOO.[17]

Safety/Toxicity

The majority of the studies report an absence of any significant adverse effects of Pygeum, although there have been rare complaints of diarrhea, constipation, dizziness, gastric pain, and visual disturbances.[4,5] One study demonstrated continued satisfactory safety profiles in 174 human subjects after 12 months of 100 mg daily doses.[12] Toxicological studies have likewise shown very good tolerability after oral administration. Administration of Pygeum to dog and rat subjects equivalent to 560 times the therapeutic dose for six-month periods resulted in no adverse effects on hematological, biochemical, or anatomical/pathological parameters. The extract had no effect on fertility in male rats and rabbits at doses up to 80 mg/kg/day – a safety margin of 50 times the therapeutic dose. Furthermore, *in vivo* and *in vitro* mutagenicity studies showed a complete absence of mutagenic or clastogenic potential. In fact, many of the constituents of Pygeum have anticarcinogenic and antimutagenic properties *in vitro* and *in vivo*.[3]

Dosage

P. africanum extract is usually administered at a dose (standardized to contain 14% triterpenes including beta-sitosterol and 0.5% n-docosanol) of 50-100 mg twice daily.[18] The efficacy of Pygeum extract at 50 mg twice daily and 100 mg once daily has been shown to be equivalent.[12]

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