Saw palmetto and lower urinary tract symptoms in men

CHARLES CHABERT MB ChB, MRCS
ZIV MAIANSKI MD
PHILLIP STRICKER MB BS, FRACS

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Herbal therapies aimed at treating lower urinary tract symptoms in men have increased in popularity. Despite this, evidence for their effectiveness is not conclusive.

Approximately half of all men aged over 50 years experience lower urinary tract symptoms (LUTS) due to benign prostatic hyperplasia (BPH). There has been a dramatic increase in the popularity of herbal therapies targeting subjective improvement in mild to moderate LUTS, due to the impact on quality of life experienced by men with BPH. These natural products are also popular because they are perceived to be efficacious with minimal side effects.

Pygeum extracts, stinging nettle root extracts, pumpkin seed oil and extracts of saw palmetto fruits are the four most commonly used plant materials found in herbal remedies for the treatment of BPH-associated LUTS in men. The most commonly used agent is saw palmetto, an extract derived from the berry of the American dwarf palm tree *Serenoa repens*, a native plant of south-eastern coastal regions of the USA. This herbal extract is widely used in Europe and the USA. According to a study published in 2004, approximately 2.5 million US adults were using saw palmetto.[1] In Europe, where the use of herbal therapies is extensive, German urologists tend to preferentially prescribe plant extracts over synthetic agents when treating BPH.[2]

A major problem in assessing the clinical effectiveness of herbal preparations such as saw palmetto is the lack of product standardisation. Significant differences are found among products in terms of their extract content and purity. Therefore, research findings about the effectiveness of one product cannot be reliably generalised to all preparations.

How does saw palmetto work?

The most widely used and studied saw palmetto preparation in Europe is Permixon (Pierre Fabre Medicament, France), a hexane extract of the American dwarf palm tree. It consists of 90% free and 7% esterified fatty acids in addition to small amounts of sterols, polyprenic compounds, flavonoids and other compounds.[3]

Permixon is not currently available in Australia, but patients may be able to buy the herbal remedy over the internet. It should be remembered that patients using saw palmetto preparations available in Australia will be using nonstandardised preparations with variations in dose and purity.

Basic research into the extract's mechanisms of action has mainly been performed using Permixon as it is a standardised product containing 160 mg of saw palmetto. While conclusive evidence regarding its mode of action remains elusive, there are several current theories, including:

- 5-alpha reductase inhibition
- inhibition of dihydrotestosterone binding to membrane receptors
- inhibition of oestrogen receptors
- alpha receptor blockade
- antioedema effects.

Both type 1 and type 2 isoenzymes of 5-alpha reductase exist within the human prostate. Both isoenzymes are responsible for catalysing the conversion of testosterone to its active metabolite, dihydrotestosterone. Although the exact aetiology of BPH has yet to be determined, it is

Dr Chabert is a Laparoscopic Urology Fellow at the Royal Surrey County Hospital, Guildford, England. Dr Mainski is a Urology Fellow at St Vincent's Hospital, Sydney. Associate Professor Stricker is Chairman, Department of Urology, St Vincent's Clinic, and Associate Professor (Conjoint), Department of Surgery, University of New South Wales, Sydney, NSW.

know that castrated men do not develop the condition, implying a direct relationship with dihydrotestosterone levels.

Several studies, including the Medical Therapy of Prostatic Symptoms (MTOPS) Study, have identified that treatment with the synthetic 5-alpha reductase inhibitor finasteride (Proscar) results in a reduction in prostate size, a 50% reduction in serum prostate specific antigen (PSA) levels and improvement in lower urinary tract symptoms. In addition, when combined with alpha blockade, finasteride can also alter disease progression in BPH.[4]

Despite the widely accepted belief that saw palmetto exerts its action primarily through 5-alpha reductase inhibition, there is still no conclusive evidence supporting this view.[3] In addition, saw palmetto does not result in the clinical and biochemical changes produced by finasteride (Proscar).

Saw palmetto is also thought to exert an effect by inhibiting the ability of dihydrotestosterone to bind to the cytosolic membrane, although this has only been shown in limited *in vitro* studies.

Other proposed mechanisms for how the extract might work include inhibition of prolactin stimulated prostatic growth, fibroblast inhibition and possible antioedema effects. Overall, despite the theoretical mechanisms proposed to account for the symptom improvement experienced by some patients while taking saw palmetto, only limited data exist to support the claims.

How effective is saw palmetto?

Several randomised controlled trials have examined the efficacy of saw palmetto, but a unified conclusion about its effectiveness has yet to be reached.

A 2004 meta-analysis of the clinical data assessing Permixon's effectiveness in treating BPH included 14 randomised controlled trials and three open label trials involving a combined total of 4280 patients. The study group concluded that based on the available data, Permixon use led to a significant improvement in peak urinary flow rates, a reduction in nocturia and a reduction in prostate symptoms scores compared with placebo.[5]

More recently in 2006 however, a randomised double-blind trial involving 225 men aged over 49 years with LUTS compared the use of 160 mg saw palmetto extract twice daily with placebo. The researchers found no significant difference between treatment and placebo groups in relation to symptom scores, maximal flow rates, prostate size, postvoid residual volume, quality of life or serum PSA levels. The side effect profile was similar between the treatment and placebo groups.[6]

There are several factors that have been put forward to explain the contradiction in results between the meta-analysis and the randomised trial, including the following:

- the effect of blinding was not assessed in many of the studies included in the meta-analysis and if this was inadequate, it could have resulted in an exaggeration of saw palmetto's benefits
- the concentration of active ingredient present within the formulations studied may have varied, leading to differing efficacy.

Although no strict guidelines exist regarding the content of saw palmetto, it has been recommended that the extract contain over 80% fatty acids and sterols. The extract used in the 2006 study contained over 90% of these compounds, which could have had an effect on the findings.

Is saw palmetto safe?

Despite conflicting study findings, saw palmetto is associated with a minimal side effect profile. There have been no reported serious adverse events linked with the extract and no effect on serum PSA has been observed. The most commonly reported non-serious side effects include diarrhoea, rash and abdominal discomfort. These finding have been confirmed by large clinical studies of men with BPH.[6]

Conclusion

There are no convincing data to support the use of saw palmetto as a clinically efficacious medical option for the treatment of BPH. Although the recent meta-analysis demonstrated improved symptom scores and flow rates with the use of saw palmetto, the studies included were limited by small patient numbers and short follow up.[5] The more recently published randomised controlled trial does not demonstrate an objective improvement in LUTS but it also had similar limitations.[6] Until more robust data from large clinical studies are available, patients must be made aware of the limitations of this treatment option. However, they should also be reassured about its safety profile if they choose to use this herbal treatment. MT

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