# 562 Urodynamic effects of the hexanic extract of Serenoa repens in patients with lower urinary tract symptoms associated with benign prostatic hyperplasia

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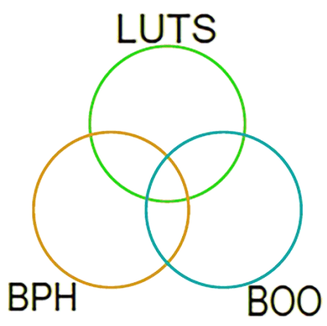
## Introduction

Lower urinary tracts symptoms (LUTS) are prevalent in adult men and are often associated with the presence of benign prostatic hypeplasia (BPH) and bladder outlet obstruction (BOO) due to benign prostatic enlargement.




Different Serenoa repens extracts (S. repens) is the phytotherapeutic agents most commonly used to treat LUTS/BPH.

Systematic reviews and meta-analyses of S. repens data from RCTs have reported different results.

In a Cochrane meta-analysis Tacklind et al. concluded that different extracts of S. repens does not improve LUTS or maximum urinary flow rate (Qmax) compared with placebo in men with LUTS/BPH [1].

It was found that different brand extracts of S repens is different by composition and free fatty acid concentration table 1, fig 2 [2,3].

**Table 1 – Composition of 14 different brands of *Serenoa repens***

| Product | FFA (mean %) | Methyl and ethyl esters (mean %) | Long-chain esters (mean %) | Glycerides (mean %) | Unsaponified matter (mean %) |
|---|---|---|---|---|---|
| Permixon | 80.7 | 2.5 | 1.36 | 6.8 | 2.27 |
| Prosteren | 74.0 | 3.7 | 1.3 | 10.8 | 2.37 |
| Saba | 70.25 | 2.85 | 1.2 | 14.4 | 2.15 |
| Rilaprost | 68.8 | 2.4 | 1.0 | 21.43 | 1.87 |
| Prostess | 68.4 | 9.5 | 1.2 | 10.6 | 2.6 |
| Sita | 62.9 | 9.35 | 1.3 | 13.45 | 2.2 |
| Quanterra prostate | 63.1 | 6.3 | 1.03 | 19.55 | 1.9 |
| Ratiopharm uno | 62.3 | 4.25 | 0.9 | 24.25 | 1.6 |
| Talso uno | 61.4 | 4.4 | 0.8 | 25.3 | 1.8 |
| Prostamol uno | 59.3 | 12.6 | 0.97 | 15.37 | 2.4 |
| Prostagutt uno | 59.2 | 9.25 | 0.85 | 19.7 | 2.0 |
| Strogen uno | 54.8 | 6.6 | 1.2 | 27.1 | 2.4 |
| Prosta-urgenine | 54.05 | 16.7 | 0.7 | 16.55 | 2.2 |
| Solaray | 40.7 | 1.5 | 0.9 | 52.15 | 1.6 |

Adapted from [4] with permission from Macmillan Publishers Ltd. FFA – free fatty acid.

Adapted with permission from Habib FK, Wyllie MG. Not all brands are created equal: a comparison of selected components of different brands of Serenoa repens extract. Prostate Cancer Prostatic Dis 2004;7:195–200

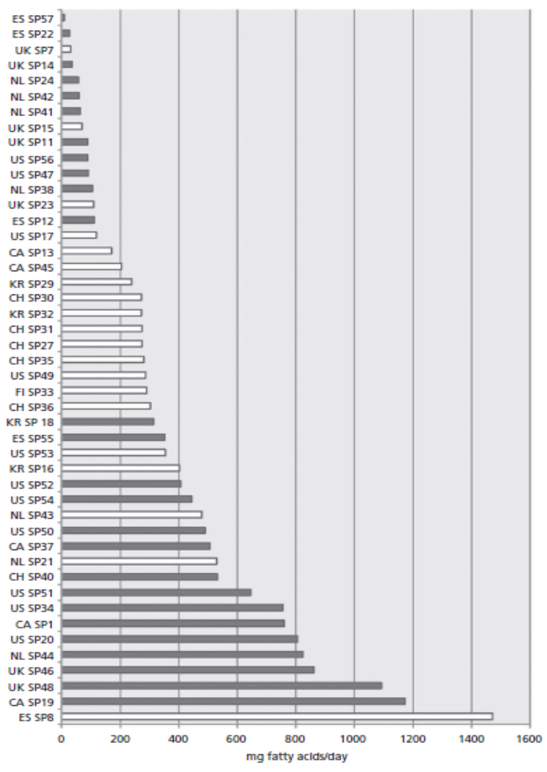



**Figure 1** Daily dose of fatty acids based on the lowest daily dosage given on the package for each product analysed. White bars indicate monopreparations containing only saw palmetto as active constituent, dark bars combination preparations that in addition contain other ingredients like vitamins or other herbal extracts. For each product, the country and the specimen number are given.
Adapted with permission from BookerA, Sutera A, Krnjic A. et al.A phytochemical comparison of saw palmetto products using gas chromatography and 1H nuclear magnetic resonance spectroscopy metabolomic profilinig. Journal of Pharmacy and Pharmacology, 2014. 66, pp. 811–822

The assessment report of the S. repens by European Medicine Agency (EMA) 2015 find out that the activity can differ from one extract to another, probably dependent upon type of extraction and the content of fatty acids [4].

Only hexane extract of S.repens (HESr) was recognized EMA as a well-established medicinal product was with proved efficacy and acceptable safety.

Systematic review and meta-analysis Vela-Navarrete et al. (2018) [5] concluded that HESr improve LUTS or maximum urinary flow rate (Qmax) compared with placebo in men with LUTS/BPH and has comparable symptomatic and objective effects with alfa-blockers [3]. It was shown that treatment by alfa-blockers or 5 alfa reductase inhibitors lead to decrease bladder outlet obstruction on 20-35%. But there is lack data of urodynamic effect HESr. The aim of study was to evaluate the urodynamic and symptomatic impact of the HESr (Permixon®) in the treatment of patients with LUTS/BPH.

## Methods

This study was pilot, single center, prospective, randomized, single blinded, placebo controlled. A total of 75 patients, aged 51,2 ± 7,9 years with mild/moderate LUTS according International Prostate Symptom Score (I-PSS) were included in the study, of which 60 patients received Permixon 320 mg daily for 12 weeks. The control group (n=15) receive placebo and did not received any medical treatment for LUTs. Patients were randomized into the study groups by investigator.

Patients were included in the study if they had mild/moderate BPH according to their mean International Prostate Symptom Score (I-PSS) (<19 points), a residual urine volume less than of 100 ml, maximum urinary flow (Qmax) more than 5 ml/s but less than 15 ml/s, no indications for emergency BPH treatment.

Exclusion criteria were the presence of urinary tract infections, suggestion of prostate cancer (PSA>4 ng/ml), urological disease affecting micturition, previous urological surgery, detrusor overactivity, neurogenic bladder, concomitant neurogenic disease and renal or liver insufficiency. Patients were also excluded if they were taking concomitant medication that might interfere with study medication, including other 5alfa-reductase inhibitors, alfa blockers, cholinolytics and antidepressants.

At the initial visit, each patient completed the I-PSS questionnaire and their medical history and concomitant medications were recorded. Prostatic volume evaluation, free flow uroflowmetry were assessed at baseline and at the end of the 12-week treatment. Cystometry and pressure/flow study with a 7F urethral catheter was performed in Medtronic Duet urodynamic equipment. The methods used conformed to the standards of the International Continence Society.

## Results

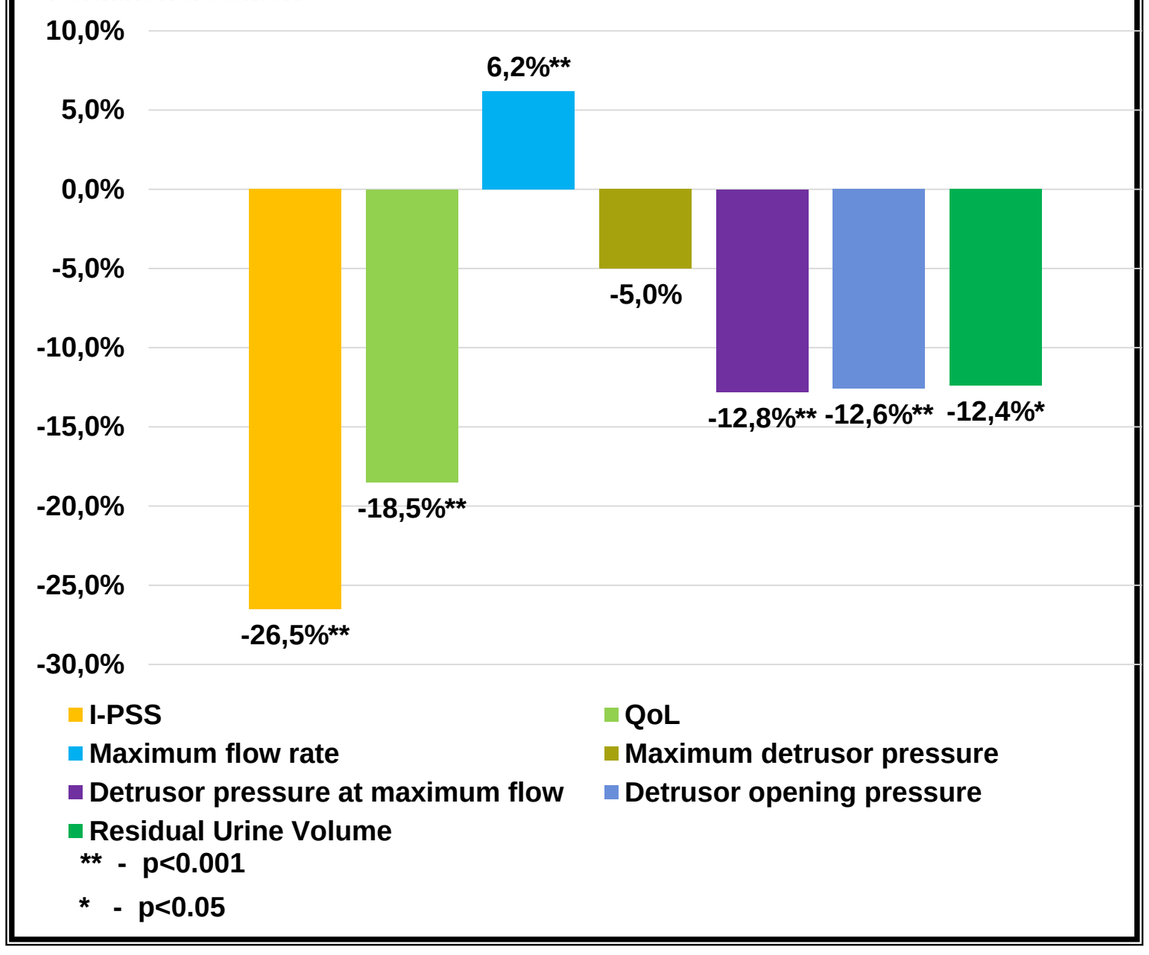
There was no significant difference between the two treatment groups at baseline in age and duration of BPH. The mean age of patients in the treatment group was 62.1 (52 ± 78) years, while the mean age of the control group was 62.9 (53 ± 78) years. The mean duration of BPH in both groups was 19.31 (3 ± 84) months.

Treatment with HESr resulted in a significant improvement in symptoms from baseline: I-PSS total score decreased by 26.5% from a baseline of 8.3 points (P<0.001) and the quality of life (QoL) score decreased by 18.5% from a baseline of 3.3 points (P<0.001).

In addition there was a significant decrease of 12.6% from baseline 59.4 centimeters of water column (P<0.001) in detrusor opening pressure and of 12.8% from baseline 73.3 centimeters of water column (P<0.001) in DP at maximum flow in patients receiving HESr.

None of these parameters improved significantly in control patients. Qmax increased by 6.2% (0.7 ml/s) from a baseline value of 11.7 (P<0.001) in the HESr group. The volume of residual urine in this group also decreased by 12.4% from a baseline value of 49.4 (P<0.05). Prostate volume after HESr treatment (71.6 ml) did not change. There were also improvement in maximum DP (5.2%) in the HESr group which did not reach significance (p=0.07). After 12 weeks there was no significant difference in mean I-PSS score, QoL score, Qmax, residual volume, urodynamic parameters in the control group. Two patients receiving HESr experienced gastrointestinal disturbances but these did not lead to withdrawal or require additional therapy.

**Fig. 2 - Percentage change from baseline in urodynamic parameters after Permixon treatment**




## Interpretation of results

HESr therapy produced a rapid and significant improvement in the majority of urodynamic and symptomatic assessments carried out in this study. There were significant reductions in the I-PSS and QoL scores, which were accompanied by significant improvements in two urodynamic parameters: DP at maximum flow and DP opening pressure. Considered together with the signify cant improvement in Qmax and residual urine, these data confrm that HESr produced an improvement in IVO. There were no significant improvements for any of these parameters in the control group despite the fact that both groups were comparable at baseline. The rapid improvement in IVO seen with HESr confirms the positive effects of the drug on urinary function and this may be mainly due to its anti-inflammatory and antioedematic action. Although this was an open-label study, the degree of improvement in the test parameters suggests
that HESr may have greater efficacy when evaluated under well-controlled conditions in patients. In contrast to our findings, a previous study which included 50 men with LUTS suggestive of BPH found that another commercially available Saw palmetto (Serenoa repens) extract did not have a significant effect on urodynamic parameters [6]. However, plant extracts strongly differ in composition according to their method of manufacture.

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## Conclusions

Treatment of LUTS/BPH with HESr produced a improvement in urodynamic parameters and symptoms, illustrating a reduction in bladder outlet obstruction. These data demonstrate that HESr is well tolerated and support its efficacy as first-line phytotherapeutic agent in patients with uncomplicated symptomatic BPH.

## References

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