

## REVIEW - SUPPLEMENTARY MATERIAL

# Non-surgical management of BPH: An updated review of current literature and state of the art on natural compounds and medical therapy

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	Study	Population	Intervention	Comparison	Stated outcome/findings
10	Jacobsen SJ, Jacobson DJ, Girman CJ, et al. Treatment for benign prostatic hyperplasia among community dwelling men: the Olmsted County study of urinary symptoms and health status	2115 men	Instrumental follow up	No instrumental follow up	Urological measurements may have influenced treatment decisions.
11	Wasson JH, Reda DJ, Bruskewitz RC, Elinson J, Keller AM, Henderson WG. A comparison of transurethral surgery with watchful waiting for moderate symptoms of benign prostatic hyperplasia. The Veterans Affairs Cooperative Study Group on Transurethral Resection of the Prostate. N Engl J Med.	800 men	Surgery	Watchful waiting	Surgery is more effective than watchful waiting in reducing the rate of treatment failure and improving GU symptoms.
13	Brown CT, Yap T, Cromwell DA, et al. Self management for men with lower urinary tract symptoms: randomised controlled trial. BMJ. 2007 Jan	140 men	Self management and standard care	Standard care alone	Self management reduced the frequency of treatment failure and reduced urinary symptoms.
20	Barry M.J., Meleth S., Lee J.Y., et al. Effect of Increasing Doses of Saw Palmetto Extract on Lower Urinary Tract Symptoms: A Randomized Trial. JAMA. 2011	369 men	1,2,3 doses of saw palmetto extract	placebo	Increasing doses of saw palmetto fruit extract did not reduce lower urinary tract symptoms more than placebo.
27	Crocerosa F, Cantiello F, Bagalá L, et al. Clinical Effects of Oral Supplementation of Gamma-Cyclodextrin Curcumin Complex in Male Patients with Moderate-To-Severe Benign Prostatic Hyperplasia-Related Lower Urinary Tract Symptoms. Urol Int. 2023	290 men	Qurmin (cavacurmin)	Standard care	Cavacurmin led to significant improvements in symptoms burden, uroflow parameters and QoL, without significant side effects.
30	Yasumoto R, Kawanishi H, Tsujino T, et al. Clinical evaluation of long-term treatment using cernitin pollen extract in patients with benign prostatic hyperplasia. Clin Ther. 1995 Jan-Feb	79 men	Cernitin pollen extract	Standard care	Cernitin pollen extract showed a mild beneficial effect on prostatic volume and urination variables in patients with symptomatic BPH

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33	Cai T, Luciani LG, Caola I, et al. Effects of pollen extract in association with vitamins (DEPROX 500®) for pain relief in patients affected by chronic prostatitis/chronic pelvic pain syndrome: results from a pilot study. <i>Urologia</i> . 2013 Apr 24	20 men	Deprox 500 2 tablets single dose daily for 30 days	Watchful waiting	Deprox 500 improved total chronic pain symptoms
35	Maurizi A, De Luca F, Zanghi A, et al. The role of nutraceutical medications in men with non bacterial chronic prostatitis and chronic pelvic pain syndrome: A prospective non blinded study utilizing flower pollen extracts versus bioflavonoids. <i>Arch Ital Urol Androl</i> . 2019 Jan	68 patients	Deprox	Quercetin based extract	Deprox demonstrated a significant improvement of symptoms
36	Maurizi A, De Luca F, Zanghi A, et al. The role of nutraceutical medications in men with non bacterial chronic prostatitis and chronic pelvic pain syndrome: A prospective non blinded study utilizing flower pollen extracts versus bioflavonoids. <i>Arch Ital Urol Androl</i> . 2019 Jan	128 men	Angustifolium extracts	none	Angustifolium extracts can be used in subjects with BPH to improve QoL
50	Nickel JC, Fradet Y, Boake RC, et al. Efficacy and safety of finasteride therapy for benign prostatic hyperplasia: results of a 2-year randomized controlled trial (the PROSPECT study). PROscar Safety Plus Efficacy Canadian Two year Study. <i>CMAJ</i> . 1996 Nov 1;155(9):1251-9. PMID: 8911291; PMCID: PMC1335066.	613 patients	patients were given finasteride (5 mg/d) for 2 years	Placebo for 2 years	Benefits and safety of treatment

	Study	Population	Intervention	Comparison	Stated outcome/findings
53	Khwaja MA, Nawaz G, Muhammad S, Jamil MI, Faisal M, Akhter S. The Effect of Two Weeks Preoperative Finasteride Therapy in Reducing Prostate Vascularity. <i>J Coll Physicians Surg Pak</i> . 2016 Mar;26(3):213-5. PMID: 26975954.	80 patients	The finasteride group (Group A) was prescribed oral 5 mg of finasteride daily for 2 weeks before surgery.	The control group (Group B) did not receive any agent	Finasteride reduces microvessel density and hence prostate vascularity with only 2-week therapy and the mean MVD is clearly correlated with size of prostate.
67	Tubaro A, Batista JE, Nitti VW, et al. Efficacy and safety of daily mirabegron 50 mg in male patients with overactive bladder: a critical analysis of five phase III studies. <i>Ther Adv Urol</i> . 2017 May 10;9(6):137-154. doi: 10.1177/1756287217702797. PMID: 28588652; PMCID: PMC5444577.	771 patients	Mirabegron 50 mg (393 patients)	versus placebo (378 patients)	Mirabegron 50 mg demonstrated superiority versus placebo (treatment difference: -0.37 [95% confidence interval (CI): -0.74, -0.01]) for reducing micturition frequency; improvements in urgency and incontinence were not significantly different between mirabegron 50 mg and placebo.
73	Brock G, Broderick G, Roehrborn CG, Xu L, Wong D, Viktrup L. Tadalafil once daily in the treatment of lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) in men without erectile dysfunction. <i>BJU Int</i> . 2013 Nov;112(7):990-7. doi: 10.1111/bju.12251. Epub 2013 Aug 13. PMID: 23937669.	1089 men without ED (n = 338) and with ED (n = 751)	Tadalafil once daily in men without or with erectile dysfunction (ED)	versus placebo	Tadalafil 5 mg once daily improved BPH-LUTS in men without ED by a magnitude similar to that observed in men with ED. The adverse event profile in men without ED was consistent with that observed in men with ED.
74	Siarni P, Roehrborn CG, Barkin J, et al. Combination therapy with dutasteride and tamsulosin in men with moderate-to-severe benign prostatic hyperplasia and prostate enlargement: the CombAT (Combination of Avodart and Tamsulosin) trial rationale and study design. <i>Contemp Clin Trials</i> . 2007 Nov;28(6):770-9. doi: 10.1016/j.cct.2007.07.008. Epub 2007 Aug 2. PMID: 17761460.	4838 patients	Combination therapy with dutasteride and tamsulosin	versus the monotherapies	Combination therapy was significantly superior to tamsulosin monotherapy but not dutasteride monotherapy at reducing the relative risk of AUR or BPH-related surgery. Combination therapy was also significantly superior to both monotherapies at reducing the relative risk of BPH clinical progression. Combination therapy provided significantly greater symptom benefit than either monotherapy at 4 yr.

	Study	Population	Intervention	Comparison	Stated outcome/findings
75	Roehrborn CG, Oyarzabal Perez I, Roos EP, et al. Efficacy and safety of a fixed-dose combination of dutasteride and tamsulosin treatment (Duodart®) compared with watchful waiting with initiation of tamsulosin therapy if symptoms do not improve, both provided with lifestyle advice, in the management of treatment-naïve men with moderately symptomatic benign prostatic hyperplasia: 2-year CONDUCT study results. <i>BJU Int.</i> 2015 Sep;116(3):450-9. doi: 10.1111/bju.13033. Epub 2015 Jan 29. PMID: 25565364.	742 patients	FDC (369 patients) followed for 24 months.	versus WW-All (373) followed for 24 months.	FDC therapy with dutasteride and tamsulosin, plus lifestyle advice, resulted in rapid and sustained improvements with significantly greater symptom and QoL improvements and a significantly reduced risk of BPH progression compared with WW plus initiation of tamsulosin as per protocol.
77	Kakizaki H, Lee KS, Yamamoto O, et al. Mirabegron Add-on Therapy to Tamsulosin for the Treatment of Overactive Bladder in Men with Lower Urinary Tract Symptoms: A Randomized, Placebo-controlled Study (MATCH). <i>Eur Urol Focus.</i> 2020 Jul 15;6(4):729-737. doi: 10.1016/j.euf.2019.10.019. Epub 2019 Nov 11. PMID: 31718957	568 patients	The mirabegron add-on therapy to tamsulosin	versus placebo, as add-on to tamsulosin.	The mirabegron add-on therapy to tamsulosin for 12 wk in men with LUTS and OAB symptoms demonstrated superior efficacy to placebo and was well tolerated.
86	Sebastianelli A, Spatafora P, Frizzi J, et al. Which Drug to Discontinue 3 Months After Combination Therapy of Tadalafil plus Tamsulosin for Men with Lower Urinary Tract Symptom and Erectile Dysfunction? Results of a Prospective Observational Trial. <i>Eur Urol Focus.</i> 2021 Mar;7(2):432-439. doi: 10.1016/j.euf.2019.09.015. Epub 2019 Oct 10. PMID: 31606473.	50 patients	25 patients discontinued tamsulosin (Group TAD)	versus 25 patients discontinued tadalafil (Group TAM).	After 12 wk of combination therapy, monotherapy with tadalafil for further 12 wk allows to preserve the improvement of storage IPSS and IIEF-5, in addition to total IPSS.