

6. Supplementary Materials

HESr Monotherapy Clinical Trials (in chronological order)

These citations appear as references [44–91] in the Reference section.

1983

1. Boccafoschi, C.; Annoscia, S. [Comparison of *Serenoa repens* extract and placebo in a controlled clinical trial in patients with prostatic adenomatosis.] *Urologia* **1983**, *50*, 1–14, doi: 10.1177/039156038305000615.
2. Cirillo-Marucco, E.; Pagliarulo, A.; Tritto, G.; Piccinno, A.; Di Rienzo, U. [*Serenoa repens* extract (Permixon®) in the early treatment of prostatic hypertrophy.] *Urologia* **1983**, *50*, 1269–1277, doi: 10.1177/039156038305000616.
3. Emili, E.; Lo Cigno, M.; Petrone, U. [Clinical results on a new drug in prostate hypertrophy therapy (Permixon).] *Urologia* **1983**, *50*, 1042–1048, doi: 10.1177/039156038305000517.
4. Mandressi, A.; Tarallo, U.; Maggioni, A.; Tombolini, P.; Rocco, F.; Quadraccia, S. [Medical treatment of benign prostatic hyperplasia: efficacy of the extract of *Serenoa repens* (Permixon) compared to that of the extract of *Pygeum africanum* and a placebo.] *Urologia* **1983**, *50*, 752–758, doi: 10.1177/039156038305000414.

1984

5. Champault, G.; Patel, J.C.; Bonnard, A.M. A double-blind trial of an extract of the plant *Serenoa repens* in benign prostatic hyperplasia. *Br J Clin Pharmacol* **1984**, *18*, 461–462, doi: 10.1111/j.1365-2125.1984.tb02491.x.

1985

6. Cukier, J.; Ducassou, J.; Le Guillou, M.; Leriche, A.; Lobel, B.; Toubol, J. [Permixon versus placebo: results of a multicenter study.] *C R Ther Pharmacol Clin* **1985**, *4*, 15–21.
7. Tasca, A.; Barulli, M.; Cavazzana, A.; Zattoni, F.; Artibani, W.; Pagano, F. [Treatment of obstructive symptomatology caused by prostatic adenoma with an extract of *Serenoa repens*: double-blind clinical test v. placebo.] *Minerva Urol Nefrol* **1985**, *37*, 87–91, PMID: 2413558.
8. Tosto, A.; Rovereto, B.; Paoletti, M.C.; Rizzo, M.; Nicolucci, A.; Costantini, A. [*Serenoa repens* extract in the treatment of functional disorders secondary to adenoma of the prostate: considerations on 20 cases.] *Urologia* **1985**, *52*, 536–542, doi: 10.1177/039156038505200410.

1986

9. Cabasino, S.; Puddu, A.; Spiga, E. [Evaluation of the efficacy of the *Serenoa repens* extract in the medical therapy of benign prostatic hypertrophy.] *Urologia* **1986**, *53*, 535–538, doi: 10.1177/039156038605300409.
10. Mancuso, G.; Guillot, F.; Migaleddu, V.; Satta, U. [*Serenoa repens* in the medical treatment of benign prostatic hypertrophy: our experience.] *Urologia* **1986**, *53*, 709–714, doi:10.1177/039156038605300511.
11. Martorana, G.; Giberti, C.; Pizzorno, R.; Natta, G.D.; Brancadoro, M.T.; Barreca, T.; Rolandi, E.; Isotta, A.; Neumaier, C.E. [Long-term study with *Serenoa repens* extract in patients with prostatic adenoma.] *Urologia* **1986**, *53*, 366–369, doi: 10.1177/039156038605300310.
12. Paoletti, P.P.; Francalanci, R.; Tenti, S.; Paoletti, G.; Pedaccini, P. [Medical treatment of prostatic hypertrophy: experience with the therapeutic use of *Serenoa repens*.] *Urologia* **1986**, *53*, 182–187, doi: 10.1177/039156038605300204.
13. Pannunzio, E.; D'Ascenzo, R.; Giardinetti, F.; Civili, P.; Persichelli, E. [*Serenoa repens* vs. gestonorone caproate in the treatment of benign prostatic hypertrophy: randomized study.] *Urologia* **1986**, *53*, 696–705, doi: 10.1177/039156038605300509.
14. Pescatore, D.; Calvi, P.; Michelotti, P. [Urodynamic assessment of treatment in patients with prostatic adenoma with *Serenoa repens* extract.] *Urologia* **1986**, *53*, 894–897, doi: 10.1177/039156038605300613.
15. Reece Smith, H.; Memon, A.; Smart, C.J.; Dewbury, K. The value of Permixon in benign prostatic hypertrophy. *Br J Urol* **1986**, *58*, 36–40, doi: 10.1111/j.1464-410x.1986.tb05424.x.

1987

16. Authie, D.; Cauquil, J. [Assessment of the effectiveness of Permixon® in daily practice: a multicentric study.] *C R Ther Pharmacol Clin* **1987**, *5*, 3-13.
17. Ollé Carreras, J. [Our experience with hexane extract from *Serenoa repens* in the treatment of benign prostatic hypertrophy.] *Arch Esp Urol* **1987**, *40*, 310-313, PMID: 2444169.
18. Vespasiani, G.; Cesaroni, M.; Parziani, S.; Rosi, P.; Valentini, P.; Porena, M. [*Serenoa repens* in the treatment of benign prostatic hypertrophy.] *Urologia* **1987**, *54*, 145-149, doi: 10.1177/039156038705400205.
- 1988**
19. Orfei, S.; Grumelli, B.; Galetti, G. [Clinical and uroflowimetric evaluation of Permixon® in geriatrics.] *Urologia* **1988**, *55*, 373-381, doi: 10.1177/039156038805500404.
- 1991**
20. Dathe, G.; Schmid, H. [Phytotherapy for benign prostatic hyperplasia (BPH) with an extract of *Serenoa repens* (Permixon).] *Urologe B* **1991**, *31*, 223-330.
- 1993**
21. Hanuš, M.; Matoušková, M. [Alternative therapy of benign prostatic hypertrophy - Permixon (Capistan).] *Rozhl Chir* **1993**, *72*, 75-79, PMID: 7692609.
- 1995**
22. Descotes, J.L.; Rambeaud, J.J.; Deschaseaux, P.; Faure, G. Placebo-controlled evaluation of the efficacy and tolerability of Permixon® in benign prostatic hyperplasia after exclusion of placebo responders. *Clin Drug Invest* **1995**, *9*, 291-297, doi: 10.2165/00044011-199509050-00007.
23. Ebbinghaus, K. [Effectiveness of Permixon for the treatment of benign prostatic hyperplasia.] *J Urol Urogynäkol* **1995**, *2*, 17-21.
24. Gorilovsky, L.M. [Permixon in the treatment of benign prostatic hyperplasia.] *Ter Arkh* **1995**, *67*, 62-64, PMID: 7482341.
- 1996**
25. Carraro, J.C.; Raynaud, J.P.; Koch, G.; Chisholm, G.D.; Di Silverio, F.; Teillac, P.; Da Silva, F.C.; Cauquil, J.; Chopin, D.K.; Hamdy, F.C., et al. Comparison of phytotherapy (Permixon) with finasteride in the treatment of benign prostate hyperplasia: a randomized international study of 1,098 patients. *Prostate* **1996**, *29*, 231-240, doi: 10.1002/(SICI)1097-0045(199610)29:4<231::AID-PROS4>3.0.CO;2-E.
- 1997**
26. Foroutan, F. [Effectiveness and tolerability of Permixon in a larger patient population (592 patients) under practical conditions.] *J Urol Urogynäkol* **1997**, *2*, 17-21.
- 1999**
27. Stepanov, V.N.; Siniakova, L.A.; Sarrazin, B.; Raynaud, J.P. Efficacy and tolerability of the lipidosterolic extract of *Serenoa repens* (Permixon) in benign prostatic hyperplasia: a double-blind comparison of two dosage regimens. *Adv Ther* **1999**, *16*, 231-241, PMID: 10915398.
- 2000**
28. Al-Shukri, S.H.; Deschaseaux, P.; Kuzmin, I.V.; Amdiy, R.R. Early urodynamic effects of the lipido-sterolic extract of *Serenoa repens* (Permixon®) in patients with lower urinary tract symptoms due to benign prostatic hyperplasia. *Prostate Cancer Prostatic Dis* **2000**, *3*, 195-199, doi: 10.1038/sj.pcan.4500477.
29. Medeiros, A.S.; Verona, C.B.M.; Mattos, D., Jr.; Silva, E.G.; Fonseca, G.N.; Begliomini, H.; Pous, J.H.; Cury, J.; Costa, M.M.; Prado, M.J., et al. [Efficacy and tolerability of the extract of *Serenoa repens* in a multicentric study in patients with symptomatic benign prostatic hyperplasia.] *Rev Bras Med* **2000**, *57*, 321-324.

2002

30. Aliaev, Y.G.; Vinarov, A.Z.; Lokshin, K.L.; Spivak, L.G. [Five-year experience in treating patients with prostatic hyperplasia patients with Permixon (*Serenoa repens* "Pierre Fabre Medicament.")] *Urologiia* **2002**, *7*, 23-25, PMID: 1187796.
31. Debruyne, F.; Koch, G.; Boyle, P.; Da Silva, F.C.; Gillenwater, J.G.; Hamdy, F.C.; Perrin, P.; Teillac, P.; Vela-Navarrete, R.; Raynaud, J.P. Comparison of a phytotherapeutic agent (Permixon) with an alpha-blocker (tamsulosin) in the treatment of benign prostatic hyperplasia: a 1-year randomized international study. *Eur Urol* **2002**, *41*, 497-506, doi: 10.1016/S0302-2838(02)00066-0.
32. Giannakopoulos, X.; Baltogiannis, D.; Giannakis, D.; Tasos, A.; Sofikitis, N.; Charalabopoulos, K.; Evangelou, A. The lipidosterolic extract of *Serenoa repens* in the treatment of benign prostatic hyperplasia: a comparison of two dosage regimens. *Adv Ther* **2002**, *19*, 285-296, doi: 10.1007/BF02853174.
33. Glemain, P.; Coulange, C.; Billebaud, T.; Gattegno, B.; Muszynski, R.; Loeb, G. [Tamsulosin with or without *Serenoa repens* in benign prostatic hyperplasia: the OCOS trial.] *Prog Urol* **2002**, *12*, 395-403, PMID: 12189745.
34. Pytel, Y.A.; Vinarov, A.; Lopatkin, N.; Sivkov, A.; Gorilovsky, L.; Raynaud, J.P. Long-term clinical and biologic effects of the lipidosterolic extract of *Serenoa repens* in patients with symptomatic benign prostatic hyperplasia. *Adv Ther* **2002**, *19*, 297-306, doi: 10.1007/BF02853175.

2003

35. Vela Navarrete, R.; Garcia Cardoso, J.V.; Barat, A.; Manzarbeitia, F.; López Farré, A. BPH and inflammation: pharmacological effects of Permixon on histological and molecular inflammatory markers. Results of a double blind pilot clinical assay. *Eur Urol* **2003**, *44*, 549-555, doi: 10.1016/S0302-2838(03)00368-3.

2004

36. Debruyne, F.; Boyle, P.; Calais Da Silva, F.; Gillenwater, J.G.; Hamdy, F.C.; Perrin, P.; Teillac, P.; Vela-Navarrete, R.; Raynaud, J.P.; Schulman, C.C. Evaluation of the clinical benefit of Permixon and tamsulosin in severe BPH patients—PERMAL study subset analysis. *Eur Urol* **2004**, *45*, 773-779, doi: 10.1016/j.eururo.2004.01.015.
37. El-Demiry, M. *Serenoa repens* in the treatment of patients with symptomatic benign prostatic hyperplasia. [Abstract.] *BJU Int* **2004**, *94*, 146-147, doi: 10.1111/j.1465-5101.2004.05079.x.

2005

38. Djavan, B.; Fong, Y.K.; Chaudry, A.; Reissigl, A.; Anagnostou, T.; Bagheri, F.; Waldert, M.; Fajkovic, H.; Marihart, S.; Harik, M., et al. Progression delay in men with mild symptoms of bladder outlet obstruction: a comparative study of phytotherapy and watchful waiting. *World J Urol* **2005**, *23*, 253-256, doi: 10.1007/s00345-005-0005-7.

2012

39. Giulianelli, R.; Pecoraro, S.; Sepe, G.; Leonardi, R.; Gentile, B.C.; Albanesi, L.; Brunori, S.; Mavilla, L.; Pisanti, F.; Giannella, R., et al. [Multicenter study on the efficacy and tolerability of an extract of *Serenoa repens* in patients with chronic benign prostate conditions associated with inflammation.] *Arch Ital Urol Androl* **2012**, *84*, 94-98, PMID: 22908779.

2015

40. Latil, A.; Petrissans, M.T.; Rouquet, J.; Robert, G.; de la Taille, A. Effects of hexanic extract of *Serenoa repens* (Permixon® 160 mg) on inflammation biomarkers in the treatment of lower urinary tract symptoms related to benign prostatic hyperplasia. *Prostate* **2015**, *75*, 1857-1867, doi: 10.1002/pros.23059.

2016

41. Alcaraz, A.; Carballido-Rodriguez, J.; Unda-Urzaiz, M.; Medina-Lopez, R.; Ruiz-Cerda, J.L.; Rodriguez-Rubio, F.; Garcia-Rojo, D.; Brenes-Bermudez, F.J.; Cozar-Olmo, J.M.; Baena-Gonzalez, V., et al. Quality of life in patients with lower urinary tract symptoms associated with BPH: change over time in real-life practice according to treatment—the QUALIPROST study. *Int Urol Nephrol* **2016**, *48*, 645-656, doi: 10.1007/s11255-015-1206-7.

2020

42. Alcaraz, A.; Rodríguez-Antolín, A.; Carballido-Rodríguez, J.; Castro-Díaz, D.; Esteban-Fuertes, M.; Cozar-Olmo, J.M.; Ficarra, V.; Medina-Lopez, R.; Fernandez-Gomez, J.M.; Angulo, J.C., et al. Clinical benefit of tamsulosin and the hexanic extract of *Serenoa repens*, in combination or as monotherapy, in patients with moderate/severe LUTS-BPH: a subset analysis of the QUALIPROST study. *J Clin Med* **2020**, *9*, 2909, doi: 10.3390/jcm9092909.
43. de la Taille, A.; Bardin, L.; Castagné, C.; Auges, M.; Capronnier, O.; Chalret du Rieu, Q. [Alpha-blockers or phytotherapy as first-line treatment of LUTS/BPH in general medicine: the PERSAT non-interventional study.] *Prog Urol* **2020**, *30*, 10, 522-531, doi: 10.1016/j.purol.2020.07.001.

2021

44. Alcaraz, A.; Rodríguez-Antolín, A.; Carballido-Rodríguez, J.; Castro-Díaz, D.; Medina-Polo, J.; Fernández-Gómez, J.M.; Ficarra, V.; Palou, J.; Ponce de León Roca, J.; Angulo, J.C.; Esteban-Fuertes, M.; Cózar-Olmo, J.M.; Pérez-León, N.; Molero-García, J.M.; Fernández-Pro Ledesma, A.; Brenes-Bermúdez, F.J.; Manasanch, J. Efficacy and tolerability of the hexanic extract of *Serenoa repens* compared to tamsulosin in moderate-severe LUTS-BPH patients. *Sci Rep* **2021**, *11*, 19401. doi: 10.1038/s41598-021-98586-5.

2022

45. Alcaraz, A.; Gacci, M.; Ficarra, V.; Medina-Polo, J.; Salonia, A.; Fernández-Gómez, J.M.; Ciudin, A.; Castro-Díaz, D.; Rodríguez-Antolín, A.; Carballido-Rodríguez, J.; Cózar-Olmo, J.M.; Búcar-Terrades, S.; Pérez-León, N.; Brenes-Bermúdez, F.J.; Molero-García, J.M.; Ledesma, A.F.; Herdman, M.; Manasanch, J.; Angulo, J.C.; Group OBOTQS. Efficacy and Safety of the hexanic extract of *Serenoa repens* vs. watchful waiting in men with moderate to severe LUTS-BPH: results of a paired matched clinical study. *J Clin Med* **2022**, *11*, 967. doi: 10.3390/jcm11040967.
46. de la Taille A, Chalret du Rieu Q, Dialla O, Bardin L. [Alpha-blockers or hexanic extract of *Serenoa repens* for 6 months: sub-analysis of the PERSAT study]. *Prog Urol* **2022**, Oct 4, S1166-7087(22)00423-7.

Notes:

- Case reports or case studies were not included in the list.
- Abstracts are generally not included. The exception is reference #37 (El-Demiry, et al. 2004) only because it was included in the 2018 Vela-Navarrete meta-analysis and has been cited historically by other publications.
- The following French-language publication contains the same data as the English-language reference #5 (Champault, et al. 1984):
 - Champault, G.; Bonnard, A.M.; Cauquil, J.; Patel, J.C. [Medical treatment of prostatic adenoma. Controlled trial: PA 109 vs placebo in one hundred and ten patients.] *Ann Urol (Paris)* **1984**, *18*, 407-410, PMID: 6085231.
- Reference #32 (Giannakopoulos, et al. 2002):
 - This study uses Libeprosta, which is a trademarked name for Permixon by Pierre Fabre Medicament, France.
- The following publication contains the same data as reference #39 (Latil, et al. 2015), also known as the PERMIN study:
 - Robert, G.Y. Comparison of the effects of hexanic extract of *Serenoa repens* (Permixon) and tamsulosin on inflammatory biomarkers in the treatment of benign prostatic hyperplasia-related lower urinary tract symptoms. *Eur Urol Suppl* **2015**, *14*, e1470-e1474, doi: 10.1016/S1569-9056(15)30502-9.
 - In the following study, the authors state that the intervention, Prostagood, is a trademarked name for Permixon in Turkey. However, that is an error. Prostagood is a trademarked name for Prostagutt, an ethanolic extract, which is licensed from Willmar Schwabe by Abdi Ibrahim Pharmaceuticals in Turkey. Therefore, this study was not included in the list, despite being historically cited as a Permixon study by others. (Source: Strum SB. *Uro* **2021**, *1*, 155-179, doi: 10.3390/uro1030017.)

-
- Hizli, F.; Uygur, M.C. A prospective study of the efficacy of *Serenoa repens*, tamsulosin, and *Serenoa repens* plus tamsulosin treatment for patients with benign prostate hyperplasia. *Int Urol Nephrol* **2007**, *39*, 879-886, doi: 10.1007/s11255-006-9106-5.