Improving Men's Health with Botanicals

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Abstract

The use of herbs to prevent (primarily) and treat some major men's health concerns are reviewed. For benign prostatic hyperplasia, the roles of *Serenoa repens* (saw palmetto), *Prunus africanum* (pygeum), *Urtica dioica* (nettle) root, and *Ammi visnaga* (khella) are discussed. For prostate cancer, *Punica granatum* (pomegranate), *Allium sativum* (garlic), and *Glycine max* (soy) and other legumes—including their isoflavones—are reviewed. For two conditions related to obesity and metabolic syndrome, erectile dysfunction and secondary hypogonadism, the roles of pomegranate, *Epimedium* spp. (horny goat weed), *Panax ginseng* (Asian ginseng), *Crocus sativa* (saffron), and phytoestrogens are discussed.

Benign Prostatic Hyperplasia: Prevention and Treatment

Enlargement of the prostate is an extremely common problem that affects all men, if they live long enough, and although not all men develop symptoms as a result, many men do.[1] Rather than simply waiting for the problem to arise and then treating it, there are herbal options to help prevent it from happening. As with all the concerns discussed here, a healthy diet and lifestyle are likely significant contributors to preventing benign prostatic hyperplasia (BPH).[2,3]

Serenoa repens (saw palmetto) fruit is an Arecaceae (palm) family shrub that is prolific in Florida, where essentially all of this herb is still harvested in the wild. Numerous studies have assessed the herb's ability to treat men with BPH symptoms, and although a meta-analysis of these trials overall suggested saw palmetto was minimally effective, one has to account for the studies that compared saw palmetto to drugs approved for treatment of men with BPH.[4] In these trials—including the largest yet conducted (in 1098 men) that compared saw palmetto to the drug finasteride, and another trial that found saw palmetto and the drug synergistically shrank the prostate—saw palmetto was consistently as effective as these agents.[5,6] Either the placebo-controlled trials are flawed or, if saw palmetto truly is no more effective than placebo, the approved drugs are also actually not effective. Given the inexpensiveness of saw palmetto, ease of use, and its extremely low risk of causing even minor adverse effects, saw palmetto remains a viable clinical option until this discrepancy in the literature can be worked out.

However, these studies did not address the topic of prevention directly, and, truly, no study has been conducted in younger, healthy men to determine if saw palmetto can prevent or delay BPH. One of the longest trials on saw palmetto in men with very mild symptomatic BPH might be relevant, however: For this trial 189 men were randomized to either saw palmetto or watchful waiting for 2 years.[7] Those who took saw palmetto had half the risk (a significant difference) of developing more serious symptoms or progressing to needing surgery, compared to the men in the watchful-waiting group. Symptoms actually were reduced significantly in the saw-palmetto group, compared to the control group. Note, also, that a remarkable 10-year–long trial found no adverse effects in 38 men who took saw palmetto for the entire duration of the observation period.[8] These results suggest that it is worth considering giving saw palmetto to men in their 30s or early 40s to try to prevent BPH from developing, though trials targeted specifically to this issue need to be conducted.

The usual dose of saw palmetto is a standardized extract containing 75%–85% sterols and fatty acids (usually called a liposterolic extract), 320 mg once per day with food. Higher doses have not been more effective, and splitting the dose to 160 mg b.i.d. has not been more effective. This costs less than $10 per month in the United States to take at this dose. Clinically, freeze-dried whole fruits at a dose of 1000 mg b.i.d. have also been effective, as have tinctures (1:3 weight:volume ratio, 30% ethanol) at a dose of 2.5 mL (0.5 tsp) b.i.d. As stated, there are almost never any adverse effects with this medicine.

Prunus africanum (pygeum) bark comes from an endangered African tree in the Rosaceae family. It really produces no action different from that of saw palmetto, which is abundant and not harmed by gathering its fruit. Harvesting the bark of this African tree can be quite damaging.[9] Therefore, use of pygeum is strongly discouraged. Even when obtained from plantations, it is questionable if transoceanic shipping of the material to North America makes any sense when much more local saw palmetto is available instead. Cultivated pygeum would obviously be more sustainable for use in Eurasia and throughout Africa.

Urtica dioica (stinging nettle) root is the second best researched herb for men with BPH, although this herb is far less well-understood than saw palmetto. Stinging nettle appears to help by completely different mechanisms, including blocking the progrowth signaling of sex hormone-binding globulin and possibly as a very mild aromatase inhibitor.[10,11] In combination with saw palmetto, stinging nettle was effective for reducing symptoms long-term and was just as effective as finasteride.[12,13] The herb is extremely safe, and although it has not been studied for prevention, it makes sense to be used this way while awaiting clinical trial evidence. Stinging nettle leaf should be avoided by men with symptomatic BPH, as it is a diuretic and can worsen symptoms. The usual dose of stinging nettle root as a tincture (1:2–1:3 weight:volume, 30% ethanol) is 2.5 mL (0.5 tsp) b.i.d., and in capsules is 500–1000 mg b.i.d. (less with more-concentrated extracts).

Once BPH symptoms begin, in addition to the remedies already mentioned, more rapid and significant relief comes from using stronger spasmolytic herbs. The current author has previously written about these in more depth, but briefly, the moderately potent herb *Ammi visnaga* (khella) fruit is particularly effective in this situation, based on clinical experience.[14] At a dose of 1 mL tincture (1:3 weight:volume, 30%–50% ethanol) b.i.d.–t.i.d., khella is usually effective within 1–2 weeks. If not, either the prostate is >50 g (and either chemical 5α-reductase inhibitors such as finasteride or surgery will be needed to get it back below this point) or even stronger spasmolytics may be needed.

Prostate Cancer Prevention

Prostate cancer is one of the most common cancers in men, although most forms of it have very low lethality.[15] Although an enormous number of resources have been devoted to the prostate-specific antigen (PSA) blood test as a screening tool, this has been found wanting and is now only recommended by the United States Preventive Services Task Force for men at high risk.[16] There is no way of telling how much misery (caused by both unnecessary overtreatment of low-grade disease and necessary treatment for high-grade lesions) could have been avoided if these resources had instead been placed into prevention.

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Most herbal agents that can reduce the risk of prostate cancer—or at least the risk of aggressive prostate cancer—are really foods. *Punica granatum* (pomegranate) is a fruit native in its own family (the Punicaceae) to the Mediterranean rim, but now grows in many other places around the world. This fruit has been studied a fair amount in preliminary trials of patients with prostate cancer, although more work is clearly needed to determine its role.

Pomegranate ellagitannins are converted by the gut flora to what are believed to be the major active compounds, including urolithin A, that actually reach the prostate in therapeutic concentrations after oral ingestion of pomegranate.[17] In vitro, these compounds have numerous complex anticancer effects in the prostate.[18] In randomized, placebo-controlled clinical trials of men with prostate cancer, pomegranate juice or extracts have shown preliminary benefits.[19,20] A combination of pomegranate, broccoli, *Camellia sinensis* (green tea), and *Curcuma longa* (turmeric) rhizome extracts was also beneficial after prostatectomy in men with prostate cancer.[21] It is not known if pomegranate intake can prevent prostate cancer, but this appears to be a very safe treatment to consider in men with low-grade disease. Typical doses of juice are 4–8 oz per day and of extract 1 g b.i.d. Loose stools and upset stomach may occur at these doses unless they are taken with food.

Allium sativum (garlic) and related medicinal vegetables (onions, chives, leeks, shallots, etc.) may hold promise for preventing prostate cancer. In a meta-analysis of nine epidemiologic studies, higher intake of garlic and, to a lesser degree, other Alliaceae family vegetables significantly reduced the risk of prostate cancer.[22] Some epidemiologic trials have failed to show a protective benefit, at least for garlic capsules.[23] In a small clinical trial of 9 Turkish men with low-grade prostate cancer, aqueous garlic extract 1 mL/kg daily for 1 month was associated with a lowering of PSA, compared to baseline.[24] A very large number of studies have shown that garlic inhibits or destroys prostate cancer cells in vitro.

Glycine max (soy) and all other Fabaceae family members (legumes) contain multiple constituents that fight prostate cancer. Isoflavones, protein, and the Bowman-Birk protease inhibitor are the best characterized of these constituents.[25,26] A meta-analysis of two clinical trials found that soy intake reduces the risk of prostate cancer in men at high risk of developing the disease.[27] Higher intake of soy foods in general, tofu specifically, and the isoflavones genistein and daidzein, all lowered the risk of prostate cancer significantly in a meta-analysis of eight case-controlled trials.[28] A meta-analysis of 15 epidemiologic trials found higher soy intake protected men against prostate cancer.[29] Taken together, the evidence is becoming stronger all the time that soy, and perhaps other legumes, protect men against prostate cancer.

Such trials, however, neglect the importance of interindividual differences in response to legumes and particularly their isoflavones. This is because of the well-established fact that the gut flora must convert daidzein to *S*-equol and genistein to 5-hydroxy-*S*-equol for legumes, particularly soy, to produce many of their benefits.[30] These equol metabolites are clearly the actual molecules that are absorbed and utilized by humans.[31] The organism *Slackia isoflavoniconvertens* among others have been identified as the microbes that perform this conversion.[32] Unfortunately, most of these organisms are obligate anaerobes and not available in any known supplement or fermented food. Equol formation rates are higher in people of Asian descent who have historically higher rates of legume intake, with modest declines in equol formation in more westernized younger generations with

lower legume intake.[33,34] Other foods, particularly dairy products, also seem to encourage the presence of equol-forming bacteria.[35] Antibiotics have been shown to reduce equol formation, and their widespread use in the West may partially explain the relatively low levels of equol formation in these populations.[36]

Metabolic Syndrome, Erectile Dysfunction, and Secondary Hypogonadism

Coronary artery disease, atherosclerosis, erectile dysfunction (ED), metabolic syndrome, and diabetes mellitus are rampant and interconnected problems among men (and also, except for ED, affect women to significant degrees). ED is most often caused by atherosclerosis and is very frequently directly related to or caused by insulin resistance, metabolic syndrome, and diabetes mellitus.[37,38] Psychologic factors also play a role very commonly, and although important, this aspect of ED is beyond the scope of this discussion. Because the topic of herbs for ED has recently been covered in depth in this journal, only a brief summary of these agents is provided here.[39]

Pomegranate fruit juice, already discussed above for prostate cancer, is antiatherosclerotic and, according to one randomized trial, did significantly help men with mild-to-moderate ED, compared to placebo juice.[40] This trial ran just 2 weeks, and it is particularly surprising there was a noticeable benefit in such a brief time; longer-term treatment is almost certainly warranted. Usually 4 oz per day of juice is used and should be diluted with water, taken with food, and used cautiously for patients with diabetes, as the juice may raise blood glucose levels. Garlic and soy may also be used to treat the underlying atherosclerotic lesions, but have not been assessed for their role in helping arteriogenic ED in particular.

Epimedium brevicornum and related species (horny goat weed, *yín yán huò*) leaves are important Chinese herbs for patients with ED. Two clinical trials were conducted to assess herbal formulas featuring horny goat weed for men with mild-to-moderate ED.[41,42] Both trials showed that the herbal formulas were effective for reducing ED. This herb appears to have at least mild phosphodiesterase type 5–inhibiting constituents but also has antiatherosclerotic properties. *Crocus sativa* (saffron) stigma is an aphrodisiac, antidepressant and antiatherosclerotic that parallels some aspects of horny goat weed. Two open trials have found saffron helpful for men with ED in general, and one controlled trial found this herb helpful for men with antidepressant-induced ED.[43–45]

Another Chinese herb strongly reputed and even better documented for men with ED is *Panax ginseng* (Asian ginseng) root, a stress-relieving and antiatherosclerotic adaptogen. Red ginseng—4-year-old roots that are steamed and dried—was effective for men with arteriogenic, psychogenic, and mixed ED in a meta-analysis of seven clinical trials involving 349 men.[46,47] Although widely cultivated, the root is rarely available organically and wild populations are still under significant harvesting pressure. It appears now that the even more sustainable fruit of this plant is also helpful in men with ED.[48]

A particular type of secondary or hypogonadotropic hypogonadism frequently develops in obese men with metabolic syndrome, prediabetes, or frank diabetes. In this condition, high levels of estradiol in the patient's body (which this does not always mean that serum levels are elevated; it can just be a relative increase for that patient compared to a previous baseline), created by aromatization of testosterone in excess adipose tissue, has an outsized suppressive effect on luteinizing hormone (LH) secretion by the pituitary gland. This can result in lowered free and bioavailable testosterone levels and symptomatic hypogonadism in some men.[49,50]

Little information is available regarding the efficacy of herbs for secondary hypogonadism in this setting. Phytoestrogens, such as legumes including soy, may block the pituitary-suppressive effects of excess estradiol. In vitro, several isoflavones have been shown to increase LH production by pituitary cells while reducing follicle-stimulating hormone, which is not critical for testosterone production.[51] Supratherapeutic doses (100–250 mg/kg body weight) of equol did not produce antiandrogen effects in rats, but showed a potential to suppress LH production.[52] One study did not find any relationship between soy milk intake and serum LH or testosterone level in healthy British men, but this is not the target population with secondary hypogonadism.[53] It is unknown what effects phytoestrogens would have, but large doses (and typically only 150 mg of isoflavones per day maximum are given in adult men) should be avoided.

Conclusion

The level of information for prevention of some major, common male health issues is variable. In BPH and prostate cancer, there is evidence of a protective effect of some herbs, but in BPH, evidence for the therapeutic effects of herbs is stronger. In metabolic syndrome–related conditions such as ED, studies are suggestive that herbs may be helpful. This is unlike the situation with metabolic secondary hypogonadism for which little-to-no evidence about herbs exists. Further information is needed to determine the utility of herbs for men with common problems specific to their reproductive systems and for their endocrine health.

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