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Topic Paper

Botanical medicines for the urinary tract

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Abstract. Four important categories of urologic herbs, their history, and modern scientific investigations regarding them are reviewed. Botanical diuretics are discussed with a focus on *Solidago spp* (goldenrod) herb, *Levisticum officinale* (lovage) root, *Petroselinum crispus* (parsley) fruit, and *Urtica dioica* (stinging nettle) herb. Urinary antiseptic and anti-adhesion herbs, particularly *Arctostaphylos uva-ursi* (uva-uri) leaf, *Juniperus spp* (juniper) leaf, and *Vaccinium macrocarpon* (cranberry) fruit are reviewed. The antinephrotoxics botanicals *Rheum palmatum* (Chinese rhubarb) root and *Lespedeza capitata* (round-head lespedeza) herb are surveyed, followed by herbs for symptoms of benign prostatic hyperplasia, most notably *Serenoa repens* (saw palmetto) fruit, *Urtica dioica* root, and *Prunus africana* (pygeum) bark.

Keywords. Botanical medicine - Diuretic - Cystitis - Chronic renal failure - Benign prostatic hyperplasia

Introduction

Plants, algae, and fungi have been utilized as medicine throughout human history and probably even before humans evolved, given the practice of botanical medicine by non-human animals [*40*]. Among the many applications of herbs in medicine include the use of these agents to treat conditions of the urinary tract.

This paper will review several important categories of urologic herbs, their history, and any modern scientific investigations regarding them. Botanical diuretics, antimicrobials and anti-adhesion agents, renal protectives, and herbs for patients with benign prostatic hyperplasia will be addressed to give a sense of the depth and breadth of botanical medicine in urology. Given the impossibility of covering the enormity of the world botanical materia medica, only European and North American herbs, with a few exceptions, will be considered in this review. Note that throughout this article, the standardized

names and families listed in *Herbs of Commerce* (2nd edn) will be used [*36*].

Botanical diuretics

Numerous herbs are traditionally considered diuretic (see Table 1). Preliminary clinical trials have shown that various herbs increase urinary output both in healthy people and people with urologic disease, and they continue to be widely prescribed in Europe [*32*, *45*, *52*]. Other trials have failed to confirm a diuretic effect in healthy people [*11*]. None of these herbs have been associated with serious adverse effects. More research is warranted on those agents shown effective to date to determine if they continue to show benefits in more rigorous settings.

Table 1. Relative potency and comparative properties of herbal diuretics. Major diuretic herbs are arranged by the author’s judgment as to their relative strength

Potency	Latin name (common name)	Part used	Family	Miscellaneous notes	Commission E approved for diuresis
Strong	*Solidago spp* (goldenrod)	Herba	Asteraceae	Anti-inflammatory	Yes
	Levisticum officinale W Koch (lovage)	Radix	Apiaceae	Mild risk of photosensitivity	Yes
	Betula spp (birch)	Folium	Betulaceae	Antimicrobial, anti-inflammatory	Yes
	Petroselinum crispum (Mill) Nyman ex AW Hill (parsley)	Radix, fructus	Apiaceae	Antispasmodic, anti-inflammatory	Yes (root only)
	Apium graveolens L (celery)	Fructus	Apiaceae	Antispasmodic	No
Medium	*Taraxacum* officinale Weber ex FH Wigg (dandelion)	Folium	Asteraceae	Bitter digestive tonic	No
	Ononis campestris Koch & Ziz (restharrow)	Radix	Fabaceae	Aqueous extracts only	Yes
	Urtica dioica L (stinging nettle)	Folium	Urticaceae	Anti-inflammatory, radix for bph	Yes
Mild	*Parietaria judaica* L (pellitory-of-the-wall)	Herba	Urticaceae		No
	Galium aparine L (cleavers)	Herba	Rubiaceae		No
	Equisetum arvense L (horsetail)	Herba	Equisetaceae	Commission E also approves topical use for wounds & internal use for post-traumatic edema	Yes
	Chimaphila umbellata (L) WPC Barton (pipsissewa)	Herba	Ericaceae	Demulcent, mild antimicrobial	No

No trials have definitely proven the mechanism of action of diuretic herbs in humans. The late pharmacognocist Varro Tyler, PhD, theorized that herbs act only as aquaretics, or agents that increase water excretion without affecting renal handling of electrolytes [*66*]. Aquaretics may work by causing dilation of glomerular arterioles, thereby increasing glomerular filtration rate. Since water intake can itself have aquaretic effects, and many aquaretic herbs are taken as teas, this would partially explain variable results of clinical trials with aquaretic herbs [*46*, *47*].

Existing animal data do not support the aquaretic theory, however. Repeatedly, diuretic herbs have been shown to influence renal electrolyte handling, particularly sodium and potassium, and thus have diuretic activity [*14*, *44*]. The distinction between an aquaretic and diuretic is critical. Aquaretics are very unlikely to affect edema or hypertension since sodium chloride is the major determinant of

extracellular fluid volume and aquaretics do not influence electrolyte levels. At least one human trial has also shown that a diuretic herb, *Urtica dioica* (stinging nettle) folium, can reduce blood pressure in patients with congestive heart failure, an effect incompatible with the hypothesis that stinging nettle is only aquaretic [*26*]. Several of the best studied diuretic herbs will be reviewed in more depth here, looking both at the laboratory work investigating mechanism of action and clinical trials where they exist.

Some herbal diuretics (noted in Table 1) have been approved for use by the German Commission E for the following conditions [*3, 49*]:

- Cystitis, urethritis, prostatitis, and other lower urinary tract infections adjunctive to antimicrobial, immunomodulating, and other therapies.
- Urolithiasis, both as prophylaxis and for acute stone passage of smaller stones in otherwise healthy patients.
- Benign urinary bladder inflammation without fever.
- Dysuria due to mild urinary bladder irritation with no obvious pathological cause.

The Commission E is an expert committee formed by the German government in 1978 to evaluate herbs sold in Germany and issue official monographs regarding them. The sole herb listed as being helpful for edema is *Equisetum arvense* (horsetail), which is approved for use in Germany for "post-traumatic and static edema" [*3*]. All herbal diuretics are listed as contraindicated in cases of edema due to congestive heart or renal failure by Commission E. The Commission E did not list the reasons behind their choices and do not cite data to support or document their conclusions, and thus one must take all their recommendations with a grain of salt. Nevertheless, they provide some support for the utility of and some details on how to prescribe some of the herbal diuretics discussed more in depth below.

Solidago spp (goldenrod)

The leaf and flower of *Solidago virgaurea* L (European goldenrod), *S. canadensis* varieties (Canadian goldenrod), *S. gigantea* Aiton (early goldenrod), and related species exert fairly consistent diuretic effects clinically [*71*]. No single active constituent has been isolated from the plant; instead, multiple compounds likely contribute to its actions [*43*]. It has been demonstrated in a double-blind, randomized clinical trial to increase urine flow, though this trial has apparently only been reported at a conference and has yet to be published in a peer-reviewed journal [*4*]. This same trial showed the extract studied to be useful for treating cystitis in pregnant women.

The mechanisms of action of goldenrod have yet to be definitively determined. One animal study found that a 60% ethanol powdered extract of *S. gigantea* had minimal effects on electrolyte excretion in the urine once the electrolytes from the extract itself were taken into account [*33*]. This same extract showed anti-inflammatory activity similar to that of diclofenac and modest spasmolytic effects as well.

Clinically, goldenrod extracts are utilized as an adjunct therapy in patients with lower urinary tract infections [*3*]. It is also utilized to prevent formation of kidney stones and to help remove urinary gravel. Despite its reputation, goldenrod is not a significant aeroallergen. This concept arose because of the unfortunate simultaneity of blooming of goldenrod and ragweed. Thus, there is no particular greater need to be concerned about patients being allergic to goldenrod than any other herb. Goldenrod should be avoided in patients with known allergies to it and in patients with renal failure, but is otherwise considered safe, including for short-term use in pregnant and lactating mothers [*35*]. The

usual dose is 2-4 g/cup infused into water for 15-20 min three times daily, capsules providing a similar amount of the dried, powdered herb, or 1-3 ml tincture three times daily [*3*].

Levisticum officinale (lovage)

The major active compounds in the root of this Eurasian plant are terpenoids and coumarins. It is a member of the Apiaceae family like *Apium graveolens* (celery) and *Petroselinum crispus* (parsley), highlighting the tendency of members of this family to be diuretic. There has been little published about lovage so practically nothing is known of its specific active constituents, beneficial secondary constituents, pharmacodynamics or pharmacokinetics. Clinically it acts as a more potent diuretic than parsley, on a par with goldenrod, but lacks the anti-inflammatory aspect of goldenrod and has a milder spasmolytic effect than parsley. It is approved by the German Commission E for use in lower urinary tract infections and urinary gravel [*3*]. The usual method of preparing a tea is to decoct 2-3 g of root in a closed container in a cup of water for 15-20 min [*3*]. One cup of this is drunk three times daily. Powdered extracts lose potency rapidly and are not recommended. The usual dose of tincture is 0.5-2 ml three times daily [*18*]. Lovage is contraindicated in pregnancy, renal failure, and renal inflammation. Like parsley it contains potentially phototoxic furanocoumarins but reactions to these are almost never encountered when lovage is used properly [*35*].

Petroselinum crispus (parsley)

The humble parsley has an ancient reputation as a diuretic. The parts used are either the root or the fruit (often incorrectly termed the seed). Detailed investigations of aqueous extracts of parsley fruit extracts have been conducted in rats [*29*]. Rats fed aqueous extracts had significantly higher 24-h urine outputs compared to when they drank regular water. Mechanistic investigations suggested parsley was inhibiting Na^+/K^+-ATPase, primarily in the renal cortex, and thus interfering primarily with potassium secretion. This appeared to cause the increased urine output. Though these findings do not place parsley in the same category as any existing class of synthetic diuretic drugs, they do strongly suggest parsley has diuretic and not just aquaretic activity.

Two groups of constituents are believed to be responsible for many of parsley's effects -terpenoids, particularly apiol, and flavonoids, particularly apigenin. The volatile oil extract of parsley has shown, like its close cousin *Apium graveolens* (celery) and apiol in isolation, calcium channel-blocking activity in vitro [*39*]. This helps explain the traditional use of parsley as a carminative, or agent that relieves intestinal spasms. Apigenin from an orally-administered parsley extract has been associated with antioxidant activity in humans [*41*]. Apigenin also exerts anti-inflammatories effects in vitro [*31*].

Clinical trials were not located regarding the efficacy of parsley as a diuretic or any other indication. However, it is approved by the German Commission E for use as a diuretic as discussed above. Typically 2 g of root or fruit are decocted in a covered vessel at low heat for 10-15 min in a cup of water, and three such cups are drunk each day [*3*]. A usual dose of tincture is 2-4 ml three times daily [*18*]. Parsley should be avoided in pregnancy as apiol may stimulate uterine contractions and in renal failure or nephritis [*35*]. Parsley contains furanocoumarins that may cause photosensitivity though the quantities are so low the chance of an actual problem from internal use of medicinal doses is slight [*78*].

Urtica dioica (stinging nettle)

Stinging nettle is a globalized Eurasian weed with the unusual feature that different parts of the plant are used fairly distinctly. The leaves and seeds are used both as mild diuretics, for nonspecific support of the urinary tract, and as topical and internal anti-inflammatories while the root has been investigated as a treatment for symptoms of benign prostatic hyperplasia (discussed later). Rat studies clearly show that aqueous extracts of stinging nettle herb have diuretic and natriuretic effects [*62*]. One preliminary uncontrolled clinical trial has suggested that stinging nettle can relieve edema caused by congestive heart failure [*26*]. Further research is definitely required before any recommendations can be made about the use of stinging nettle in such situations, but this initial information supports the concept that botanicals do act as diuretics and not just aquaretics as previously mentioned.

It should be noted that there are three other categories of botanical diuretics: plants containing cardiac glycosides, plants with angiotensin-converting enzyme (ACE) inhibiting properties, and plants containing methylxanthines (see Table 2). Few of these plants are used primarily as diuretics, however, as their other properties are either more important or strong (in the case of cardiac glycosides and methylxanthines) or the effects are too weak or poorly investigated (in the case of botanical ACE inhibitors). Therefore, these are included mostly for reference but are not used as diuretics. In the case of cardiac glycosides, the diuretic effect may indeed contribute to their benefit in patients with congestive heart failure.

Table 2. Special botanical diuretics

Mechanism	Examples	Notes
Cardiac glycosides	*Digitalis purpurea* L (digitalis) folium	Used for CHF patients exclusively, and largely superseded by synthetic drugs.
	Nerium oleander L (oleander) folium	
	Apocynum cannabinum L (Indian hemp) folium	
	Adonis vernalis L (spring adonis) flos [a]	
	Urginea maritima (L) Baker (red squill) bulbus	
	Convallaria majalis L (lily-of-the-valley) herba	
ACE inhibitors	*Allium sativum* L (garlic) bulbus	Have only been proven to act in this way in vitro at present.
	Camellia sinensis L (tea) folium	
	Crataegus laevigata (Poir) DC (hawthorn) fructus, flos, & folium	
	Ganoderma lucium (Curtis Fr) P Karst (reishi) fruiting body	
	Olea europaea L (olive) folium	
Methylxanthines	*Camellia sinensis*	Rarely used in this way due to adverse effects (anxiety, insomnia, cystic breasts, etc.).
	Coffea arabica L (coffee) semen	
	Paullinia cupana Kunth (guaraná) folium	
	Cola nitida (Vent) A Chev (cola) semen	

[a] Endangered species that should not be used

Urinary antimicrobial & antiadhesion herbs

Numerous botanical medicines have antimicrobial activity. This is entirely logical when one realizes that algae, fungi, and plants are faced with continual pressure from microbiological infection, and thus evolve countermeasures. The chemical compounds botanical agents evolved to protect themselves are also often useful in preventing or treating infections in animals. Because many of these compounds are renally excreted, there tend to be many agents that are specifically useful as urinary antiseptics. There are two major mechanisms that botanical antimicrobial compounds have that will be discussed here - those that directly kill microbes and those that interfere with their adhesion to epithelium cells.

Arctostaphylos uva-ursi (uva-ursi)

Arctostaphylos uva-ursi (L) Spring (uva-ursi) is a shrub native to mountainous areas of North America, though it has spread to other parts of the world as well. It is a member of the Ericaceae family. A related and potentially stronger species from the desert regions of the southwestern United States and northern México is *Arctostaphylos pungens* Kunth (Mexican manzanita) [*38*]. The leaves are the therapeutic portion of the plant and contain the glycoside arbutoside. When arbutoside is consumed, it is hydrolyzed in the gut to glucose and the aglycone hydroquinone [*37*]. Hydroquinone is absorbed and then glucuronidated in the liver. Hydroquinone glucuronide is then carried to the kidneys where it is excreted in the urine. If the pH of the urine is sufficiently alkaline (>7), then the hydroquinone glucuronide will decompose spontaneously, releasing the hydroquinone to act as a direct antimicrobial agent [*12*]. If uva-ursi does not seem to be working, there is a possibility that the patient's urine is excessive acidic and interfering with decomposition of the hydroquinone glucuronide complex. Animal product ingestion should be decreased in the diet or 1 tablespoon sodium or potassium bicarbonate taken once or twice a day to alkalinize the urine in such situations before making a final determination about efficacy.

Women (n=57) with recurrent cystitis volunteered for a double-blind trial and were randomized to take placebo or an uva-ursi extract for 1 month [*30*]. The uva-ursi extract was standardized to unspecified levels of arbutoside and methylarbutoside. Women in the uva-ursi group had no episodes of cystitis in the following year compared to 23% of women who took placebo. No adverse effects were reported.

This trial was unusual in that uva-ursi is traditionally considered a treatment for lower urinary tract infections (UTI), not a preventive therapy. Uva-ursi is approved only for use in treating UTI, not in their prevention, by the German Commission E [*3*]. Part of the reason for this is the concern that long-term exposure to hydroquinone may be carcinogenic, based on information from industrial exposures to synthetic hydroquinone and laboratory research [*8*]. Normally, it is recommended for use for no more than 2 weeks consecutively to avoid any problems in this regard. The dose of uva-ursi recommended by the Commission E is 3 g leaf extracted in 150 ml water by either hot or cold infusion up to four times daily, providing 400-840 mg arbutoside. Hot infusions (as well as some standardized extracts) will extract the tannins in uva-ursi leaf which may cause digestive upset; cold infusions do not have this problem. Recently, a tannin from uva-ursi dubbed corilagin has been shown to potentiate the activity of beta-lactam antibiotics against methicillin-resistant *Staphylococcus aureus* in vitro [*55*]. This lends some support to the concept of using whole plant extracts as opposed to isolated arbutoside, as other constituents in uva-ursi may have synergistic effects with each other. Uva-ursi should be avoided during pregnancy and lactation, renal failure, and dyspepsia (tannin-containing extracts only) and may not be appropriate for children [*35*].

Juniperus communis and other species (juniper)

Another herb with significant antimicrobial activity is the European tree *Juniperus communis* L (juniper) folium and other closely related juniper trees such as the North American species *J. monosperma* (Engelm) Sarg (one-seed juniper) and *J. osteosperma* (Utah Juniper). Junipers are in the Cupressaceae family. Juniper leaves contain antimicrobial terpenoids that may also have diuretic activity. Terpenoid-free hexane extracts from various parts of a number of juniper species showed fairly limited antibacterial activity in vitro [*7*]. Cedrenes, types of terpenoids, were found to be the most active antimicrobial compounds in *J. occidentalis* (western juniper) [*24*]. Clinical trials have not been reported on the efficacy of juniper extracts in patients with urinary tract infections, though this is a relatively common indication in Europe [*48*]. Juniper berry is approved for treatment of dyspepsia by the German Commission E but only indirect mention is made of its use in treating UTI [*3*].

Animal studies repeatedly show that juniper extracts increase urinary volume [*19, 20*]. The mechanism of action is uncertain. Animal studies have shown that juniper leaf infusions are more diuretic than the volatile oil, suggesting that constituents other than terpenoids likely contribute to the diuretic activity of this herb [*59*]. There is a long-held belief in botanical medicine circles that juniper volatile oil contains nephrotoxic compounds, particularly hydrocarbon terpenoids such as pinenes. However, animal studies clearly show this is only true at extraordinarily high doses, far beyond the typical therapeutic realm [*51*]. Two separate reviews of published literature on juniper nephrotoxicity both conclude there are no verifiable modern reports of renal injury from therapeutic use of juniper, that older reports of this likely resulted from misidentification or adulteration of juniper oil with either turpentine or *Juniperus sabina* (savin) oil, and that older reports may also have confused proteinuria caused by renal inflammation due to underlying disease as opposed to damage caused by juniper [*50, 65*]. At present there is no substantiation of the supposed nephrotoxicity or abortifacient properties of juniper available in peer-reviewed literature. Nevertheless, juniper should be used with caution in acute pyelonephritis and probably avoided in pregnancy until more information becomes available showing it definitely safe.

Vaccinium macrocarpon (cranberry)

Vaccinium macrocarpon Ait (cranberry) fructus, a native North American bog plant in the Ericaceae family, contains proanthocyanidins that inhibit binding of *Escherichia coli* and other microbes to the bladder epithelium [*57*]. It also inhibits binding of *E. coli* to intestinal mucosa and *Helicobacter pylori* to gastric mucosa [*6, 77*]. Cranberry's close cousin the blueberry (*Vaccinium angustifolium* Ait and other species) contains similar constituents with similar anti-adhesion activity [*42*]. Cranberry was previously believed to work through acidification of the urine, but it only causes temporary if any pH changes lasting 10-15 min in most people [*25*]. Therefore ,this mechanism of action is unlikely to be of relevance. Cranberry is also extremely unlikely to interfere with the activity of uva-ursi.

One double-blind study found that cranberry juice reduced the severity of bacteriuria in elderly women compared to placebo [*2*]. The actual incidence of recurrent infection was not analyzed in this study. In a nonblinded controlled trial, cranberry juice drunk ad libitum was no more effective than a mixed berry juice without cranberry at reducing urinary tract infection rates in hospitalized elderly patients [*27*]. Because other berries may contain active procyanidins, the choice of control in this trial must be seriously questioned. A meta-analysis of available clinical trials found a lack of quality studies and an overall lack of evidence supporting the efficacy of cranberry for preventing urinary tract infections [*22*]. No controlled clinical trials have been conducted to determine the efficacy of cranberry for treatment of urinary tract infections [*21*]. The usual dose of cranberry juice in acute situations is 250-500 ml two to three times per day, or 250-500 ml daily for prevention. Unsweetened juice is preferable to avoid the adverse effects of simple sugar intake. Capsules of concentrated cranberry are also available; typical doses are 2-3 capsules two to four times daily for acute infections and 1 capsule 2-3 times daily for prevention.

Cranberry is nontoxic and safe in pregnancy in lactation, given that it is routinely consumed as food in such situations without ill effects. Recently, a tiny study (n=5) in healthy volunteers found that cranberry tablets could raise urinary oxalate levels and calcium oxalate supersaturation significantly, yet also elevated urinary magnesium and potassium levels significantly [*64*]. The authors suggested that people at risk of urolithiasis should be counseled to avoid cranberry, yet such a small study, lacking a control group, and with such mixed results is hardly a basis for making any recommendations about the safety of cranberry. The influence of cranberry on urinary stone formation is unknown at present.

Berberine

Another botanical compound that has been shown to interfere with adhesion of *E. coli* to bladder epithelium is berberine [*61*]. Berberine is an alkaloid found in plants such as *Mahonia aquifolium* (Pursh) Nutt (Oregon Grape) radix, *Hydrastis canadensis* L (goldenseal) radix, and *Coptis chinensis* Franch (goldthread) radix. These herbs are frequently used as part of protocols to treat infections throughout the body, and should be more thoroughly researched as part of a natural approach to urinary tract infections.

Antinephrotoxic botanicals

A number of botanicals have been investigated for their protective effects on renal epithelium. Some of these investigations are based on traditional use of these botanicals while others are based on extrapolations from other pharmacologic properties. An example of a herb in the latter category is *Silybum marianum* (L) Gaertn (milk thistle) semen. Apparently based on the protective effect of its flavonoids on hepatocytes, these compounds have also been tested in rats and shown to reduce the toxicity of cisplatin against renal tubular epithelium [*13*]. Two of the more intriguing renoprotective herbs will be discussed in more depth below.

Rheum palmatum (Chinese rhubarb) radix

The root of *Rheum palmatum* L (Chinese rhubarb), family Polygonaceae, has been utilized in medicine in traditional Chinese medicine for millennia. Though many *Rheum* species are utilized in medicine, *R. palmatum* consistently contains higher levels of tannins and thus is considered to be of superior quality [*63*]. Tannins in Chinese rhubarb have been shown to reduce levels of uremic toxins and to improve glomerular filtration and blood flow to the kidneys in experimental animals [*74*, *75*]. Glomerulosclerosis has been shown to be reduced after aqueous extract of Chinese rhubarb was administered to rats who underwent subtotal nephrectomy compared to those given only plain water [*79*]. Another study in rats with diabetic nephropathy found that rhubarb extract speeded nitrogen excretion and alleviated hyperlipidemia compared to control rats [*76*]. Though clearly more work is needed to determine the exact mechanisms of Chinese rhubarb extracts on the kidney, the existing laboratory and animal data strongly confirm that Chinese rhubarb is of use in preventing and at least partially reversing various kidney lesions.

Rhubarb has long held an esteemed place in traditional Chinese herbalism as part of treatment protocols for patients with chronic renal failure (CRF). Chinese rhubarb has been investigated in preliminary clinical trials in China and shown to have beneficial effects on symptoms, blood urea nitrogen and serum creatinine levels in CRF patients. In a randomized trial, Chinese rhubarb extract was found to lower total and low-density lipoprotein (LDL) cholesterol levels and increase serum high-density lipoprotein (HDL) cholesterol and albumin levels in patients with CRF compared to controls [*23*]. All subjects in this trial were undergoing hemodialysis.

A decoction of *Panax ginseng* CA Meyer (Asian ginseng) radix, *Astragalus membranaceus* (Fisch) Bunge (astragalus) radix, *Cinnamomum cassia* Nees ex Blume (cassia) cortex, *Glycyrrhiza uralensis* Fisch et DC (gan cao) radix and Chinese rhubarb was found to reduce fatigue, weakness, cold aversion, anorexia, sexual dysfunction, and mental depression compared to baseline while comprehensive Western treatment including aldehyde oxystarch did not relieve symptoms in a controlled trial of CRF patients [*54*]. BUN and creatinine levels were both lowered significantly compared to baseline by both treatments. All subjects in the trial were simultaneously undergoing hemodialysis. In a similar trial, a combined herbal protocol with Chinese rhubarb was shown to reduce

blood urea nitrogen and symptoms in patients with CRF undergoing hemodialysis compared to controls treated with hemodialysis alone [*73*].

Though more rigorous controlled trials are necessary, Chinese rhubarb extracts have significant potential to improve treatment protocols for patients with CRF. A typical dose is 3-12 g divided throughout the day of a powdered aqueous extract or mild decoction. Overdose may cause catharsis due to the presence of anthraquinone glycosides in the herb.

Lespedeza capitata (round-head lespedeza) herb

Far less researched than Chinese rhubarb is *Lespedeza capitata* Michx (round-head lespedeza) a herb of the Fabaceae family. This native North American plant has been utilized primarily in Europe as a treatment for patients with CRF. Preliminary clinical trials conducted in France suggest that injectable extracts of round-head lespedeza can reduce azotemia in patients with renal failure of various types [*9*]. The mechanism of action of round-head lespedeza has not yet been determined. One study found that procyanidins from round-head lespedeza inhibited angiotensin-converting enzyme [*69*]. It is nontoxic at typical therapeutic doses. The most common method of administration is as a tincture at a dose of 2-5 ml three times daily.

Prostatic botanicals

Symptoms related to benign prostatic hyperplasia (BPH) commonly plague men over age 50 years. The potential for kidney- and life-threatening urinary obstruction is a more grave aspect of BPH, and an ideal therapy would not only improve quality of life but also reduce the risk of obstruction and need for surgical intervention. Several botanical therapies have been well-documented to reduce symptoms of BPH. Unfortunately, no trials have yet been published assessing the impact of these therapies on long-term risk of obstruction or incidence of surgical treatment.

Serenoa repens (saw palmetto)

Serenoa repens (W Bartram) Small (saw palmetto) is a member of the Arecaceae or palm family native to the southeastern United States. The ripe fruits of the plant are utilized as medicine. Fatty acid esters are considered the most important group of constituents and oral administration of extracts rich in these compounds have been shown to inhibit intraprostatic 5-alpha reductase (5AR) in men without influencing systemic testosterone levels or prostate-specific antigen (PSA) levels [*34*]. The control group in this trial was treated with finasteride. While the saw palmetto extract inhibited 5AR by a mean 32%, finasteride inhibited it 80%. PSA levels were reduced by approximately half on average by finasteride.

In vitro studies indicate that saw palmetto extracts have much broader actions than just inhibition of 5AR. They have been shown to partially antagonize testosterone receptors and interfere with estrogen receptors in prostate cells, to relax prostatic smooth muscle, and to interfere with prolactin [*10*, *15*, *60*, *67*].

Numerous double-blind clinical trials have been conducted using extracts of saw palmetto standardized to fatty acid content in men with BPH symptoms. One meta-analysis of existing data concluded that saw palmetto extracts are as effective as finasteride at reducing symptoms and increasing uroflow measures in men with BPH while causing fewer adverse effects [*72*]. Another meta-analysis found that saw palmetto extracts are superior to placebo at improving symptoms and uroflow [*5*]. Both trials note that existing trials are still of relatively short duration and that there is

some heterogeneity in terms of the extracts tested, study design, and outcome measures. Nevertheless, some of the best data on any botanical medicine exists for saw palmetto. Given its relatively low cost compared to finasteride or alpha-adrenergic antagonist drugs, solid evidence base, and excellent safety profile, it can be heartily recommended as first-line therapy in men with mild-to-moderate symptoms of BPH. The dose used in most trials is 160 mg twice daily or 320 mg once daily. Gastric upset and sexual dysfunction occur with the same frequency in men taking saw palmetto as placebo in clinical trials [*72*].

Trials are urgently needed to determine whether or not saw palmetto has any impact on long-term complications or surgery rates in men with BPH. Saw palmetto has never been shown to reduce prostate volume, though this is not necessarily the only basis of thinking a treatment could reduce complications of BPH [*72*].

Urtica dioica (stinging nettle)

As already mentioned, *Urtica dioica* L (stinging nettle) radix has been investigated for treating symptoms of BPH. This now widely distributed Eurasia weed is an excellent source of medicine given its sustainability, though more than one hiker might curse its name after stumbling into this aptly herb.

Stinging nettle root contains lignans that directly or indirectly (through metabolites produced primarily by the gut flora) prevent testosterone binding to sex hormone-binding globulin (SHBG) [*52*]. Other constituents may contribute to the ability of root extracts to weakly inhibit 5AR and more strongly inhibit aromatase [*16*, *28*]. Aqueous root extracts inhibit binding of SHBG to its receptor on prostate cells [*17*]. Polysaccharides and lectins have also been suggested to be important constituents in the root, mediating inflammation and growth factor activities within the prostate [*70*].

In double-blind clinical trials generally less extensive and rigorous than those conducted with saw palmetto, stinging nettle root extracts have shown to significantly lower SHBG levels and improve uroflow measures in men with BPH compared to placebo [*68*]. Many trials of stinging nettle root have looked at it in combination with saw palmetto. Once such double-blind trial found the combination equally effective at reducing symptoms and increasing uroflow with fewer adverse effects than finasteride over one year's time [*58*]. The doses used in this trial were 160 mg saw palmetto and 120 mg stinging nettle extracts twice daily. Though more rigorous trials are needed, existing data suggest that stinging nettle can reduce symptoms in men with BPH. Its efficacy compared to alpha-adrenergic antagonists, finasteride, saw palmetto, and placebo should be more deeply investigated. Like saw palmetto, stinging nettle is cheap and nontoxic at usual therapeutic doses.

Prunus africana (pygeum)

Prunus africana (Hook f) Kalkman (pygeum) cortex has also received considerable research attention as a treatment for men with BPH [*1*]. This tree in the Rosaceae family is native to central Africa. Though it appears as safe and effective as saw palmetto and stinging nettle, there are serious concerns about its ecologic sustainability [*56*]. Due to lack of sufficient protections on the tree, it has been overharvested in the wild. Harvesting a bark improperly can easily kill a tree, and they are much slower to grow than those like saw palmetto or stinging nettle. Fortunately, the Italian botanical extract company Indena has created a pygeum plantation to insure the availability of a sustainable source of this medicine. Given the much wider availability of sustainable sources of equally effective botanical alternatives, however, pygeum is not recommended for routine use. It should be reserved for patients in whom the above-mentioned herbs do not work and only sustainable sources should be used in such cases.

Conclusion

A number of different botanical medicines show promise in the treatment of a variety of urologic disorders. Insufficient resources have been placed in research on most of these treatments, however, to fully understand their pharmacodynamics let alone their pharmacokinetics, efficacy in randomized trials, or safety. Existing research does suggest that many traditional herbal practices are valid and can be improved upon, leading to relatively inexpensive, effective, and safe therapies. It is hoped that greater dispersion of knowledge about and interest in botanical medicine can help reduce political obstacles to wider use of botanical remedies in many settings.

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