

Botanical supplement use and potential side effects in patients with chronic kidney disease

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Use of alternative medicine in the U.S. has increased 34% to 42% between 1990 and 1997 (1,2). Therapies increasing the most included herbal medicines, megavitamins, folk remedies and homeopathy. More recently, it was estimated that over 38 million adults in the United States used herbal products in 2002 based on responses to the complementary and alternative medicine (CAM) supplement to the 2002 National Health Interview Survey (NHIS) (3).

The popularity of botanical supplements reflects their availability without a prescription from natural food stores, supermarkets, pharmacies and via the Internet as well as the belief among consumers that these products are important to their health and well-being (3). Although they are used for "medicinal" purposes, botanical products are not regulated in the same way as prescription and over the counter medications (4). The Dietary Supplement Health and Education Act (DSHEA) classifies herbal products as dietary supplements and limits their control by the Food and Drug Administration (FDA). Consequently, these products can be marketed with limited proof of safety or effectiveness. Since quality and consistency of botanical products is affected by harvesting, storage, processing and formulating methods, there is a need for validated quality control techniques to ensure standardization of products (5). These measures would allow comparison of pharmacological, toxicological and clinical studies of botanical supplements.

When botanical supplements are taken in combination with prescribed medications, there is the potential for herb-drug interactions (6). In patients with chronic kidney disease (CKD), possible hazards of botanical supplement use

are not limited to drug interactions but also include negative effects on kidney function, exacerbation of electrolyte abnormalities and alterations in blood pressure (7).

This column will review botanical supplement use in the CKD population and summarize traditional uses and potential adverse effects of more commonly used botanical products.

Botanical supplement use in the CKD population

Since complementary and alternative medicine use is common in the general population, it is likely that patients with CKD are also trying these therapies (1-3,8). Pre-dialysis, maintenance dialysis and post-renal transplant patients may use alternative medicine in the form of botanical supplements when conventional medicine is ineffective or causes adverse side effects (9). However, there are few documented studies of herbal supplement use in this population.

In a cross-sectional survey of 100 Canadian adults (age >18 years) with renal failure (CKD Stages 2 through 5), a detailed questionnaire was used to collect information on dietary supplements used (10). Forty-five percent of respondents used dietary supplements. Garlic and cranberry juice extract were among the most commonly used products. Less commonly used herbal products (<2% of supplement users) were Noni, saw palmetto, bilberry, valerian root, flaxseed, evening primrose oil, ginseng and St. John's wort. Use of supplements was more common in the early stages of kidney disease and decreased as renal failure progressed.

Another study identified botanical product use in a maintenance dialysis population in northwest Ohio by conducting personal interviews with the patients (11). Thirty-one of the 216 peritoneal dialysis and hemodialysis patients surveyed reported taking botanical products. Use of garlic and ginseng was reported most often. Other herbal products used were aloe, alfalfa, belladonna, bilberry, black cohosh, cat's claw, corn silk, cranberry, dandelion, Echinacea, ginkgo, goldenseal, horse chestnut and saw palmetto.

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A few studies have been directed to determine beneficial effects of botanical supplements on specific symptoms in patients with CKD. In one study, 16 hemodialysis patients were randomly assigned to receive either linoleic acid or evening primrose oil rich in gamma-linolenic acid for treatment of uremic skin problems (12). Patients receiving evening primrose oil showed significant improvement in uremic skin symptoms and greater improvement in pruritis scores than those given linoleic acid. These findings suggest that evening primrose oil may be effective for treatment of uremic pruritis in hemodialysis patients.

Adverse effects of botanical supplements on renal function have also been studied. In the early 1990s, a small group of women developed renal failure after using a weight loss regimen based on a formulation of Chinese herbs. When 15 women (mean age 41 ± 10 years) with Chinese herb nephropathy were compared with a control group matched for age, sex and serum creatinine but with interstitial nephropathies of other origins, the study group showed more rapid deterioration in renal function and more severe anemia (13). Toxicological investigation of the herbal supplement revealed that the Chinese herb Fangchi (*Aristolochia fangchi*) had inadvertently been substituted for Fangji (*Stephania tetrandra*) during formulation. Aristolochic acid in Fangchi caused interstitial nephropathy in the women who followed this weight loss regimen. Although treatment with angiotensin-converting enzyme (ACE) inhibitors failed to prevent progression of renal failure in these patients, several were successfully transplanted without recurrence of renal disease. Other cases of Chinese herb nephropathy linked to aristolochic acid have been reported, underscoring the need for standardization of formulation methods and more precise labeling of herbal supplements (14-16).

Traditional uses and adverse effects of botanical supplements

Botanical supplements taken by patients with CKD may interfere with conventional medical treatment and it is important for the renal care team to understand which alternative therapies their patients are using (17). The Table lists botanical supplements that patients with CKD have reported using (10,11). Traditional uses and potential adverse effects are shown for each botanical supplement (18-33).

As shown in Table 1, interactions between botanical supplements and prescribed medications are common, and can result in serious clinical consequences. Patients taking anticoagulants are at high risk for herb-drug interactions, but botanical supplements may also interfere with the actions of other medications including antihypertensives, anticonvulsants, diuretics, immunosuppressants and cholesterol-lowering drugs. Other potential adverse effects of botanical supplements include gastrointestinal disturbances, electrolyte and fluid imbalance, hypoglycemia and hepatotoxicity.

Few consumers of botanical supplements inform conventional health care providers of their use, and 60% of current herbal supplement users in a maintenance dialysis population did not tell their nephrologist that they were taking these products (3,11). It may be difficult for patients to find reliable information on botanical supplements in a timely manner (20,34,35).

Clearly, it is vital for the renal care team to screen patients for use of botanical supplements and to provide education regarding their potential effects. Patients should be encouraged to bring in all products that they are taking for periodic medication reviews so that the care team is informed of botanical supplement use. Patients can also be educated about risks associated with specific herbal supplements. If a patient continues to take these products, some simple guidelines can be provided (18):

1. Use only those supplements that have been standardized to ensure consistency.
2. Supplements that display the United States Pharmacopeia (USP) symbol comply with the five quality criteria listed below:
 - Contain ingredients listed on the product label;
 - Contain declared amounts and concentrations of ingredients;
 - Readily broken down in the gastrointestinal tract for effective nutrient absorption;
 - Screened for harmful contaminants;
 - Manufactured in controlled conditions.
3. Inform health care providers of botanical supplement use;
4. Avoid using supplements in larger than recommended

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Table 1

Uses and potential adverse effects of botanical supplements in patients with chronic kidney disease (CKD)

Botanical Supplement	Traditional Uses (18,19)	Potential adverse effects
Aloe	Anti-inflammatory, wound healing and laxative effects	Diarrhea, hypokalemia, increased toxicity with cardiac glycosides (11,18)
Alfalfa	Alleviation of swelling, fluid retention and kidney stones	Decreased effectiveness of the anticoagulant warfarin; high potassium content may affect electrolyte balance in patients taking potassium-sparing diuretics (11,20)
Belladonna	Relief from headache, peptic ulcer disease, inflammation, menstrual symptoms	Exacerbation of congestive heart failure; tachycardia (11)
Bilberry	Treatment of urinary tract infection, kidney stones, diabetes, diarrhea	Lowers blood glucose; may increase bleeding risk when taken with non-steroidal anti-inflammatory drugs (NSAIDs) (11,21)
Black Cohosh	Relief from menstrual disorders, early menopause	Cramps, dizziness, gastrointestinal discomfort (18)
Cat's Claw	Stimulation of the immune system, anti-inflammatory effects, treatment of gastrointestinal complaints	Reduction in blood pressure and heart rate; interaction with anticoagulants (18) Report of acute kidney injury in systemic lupus erythematosus (SLE) patient (36); Fever, intermittent constipation, diarrhea, and fatigue, avoid use with immunoglobulin therapy, immunosuppressive agents and bovine or porcine insulin (36)
Corn Silk	Treatment of prostate and urinary tract infections; kidney stones	Lowers blood pressure; hypokalemia (11)
Cranberry Juice Extract	Treatment of urinary tract infections	Nephrolithiasis (11)
Dandelion	Alleviation of upset stomach, water retention, urinary tract infections, kidney stones and poor appetite; blood sugar regulation	Enhances diuretics, interferes with antacids (11)
Echinacea	Relief of cold symptoms	Interaction with anti-rejection drugs; exacerbation of autoimmune disease and Type 1 diabetes mellitus. Can cause hepatotoxicity if used for more than 8 weeks and should not be used with other hepatotoxic drugs including anabolic steroids, amiodorone, methotrexate and ketoconazole (18,22)
Evening Primrose Oil	Uremic pruritis, menstrual disorders	May cause nausea, indigestion, soft stools, increased bleeding time; inhibits inflammation; may lower seizure threshold when taken with anticonvulsants (18,22)
Flaxseed	Bulk-forming laxative	Requires increased fluid intake (23)
Garlic	Antioxidant properties; reduction of cholesterol, triglyceride and blood sugar levels; treatment of hypertension and atherosclerosis	Interacts with warfarin, increasing anticoagulant effect (21,24,25)

doses or for long periods of time;

- Avoid wild botanical, which can be misidentified or contaminated.

The safety of botanical supplements for patients with CKD is of significant concern. Further research is needed

to investigate the use of these products in this population, and the safety and effectiveness of products consumed. Efforts should be directed to provide appropriate instructional materials to educate and inform patients about bo-

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Table 1 (cont.)

Uses and potential adverse effects of botanical supplements in patients with chronic kidney disease (CKD)

Botanical Supplement	Traditional Uses (18,19)	Potential adverse effects
Ginkgo	To maintain or enhance mental function	Interacts with warfarin, increasing anticoagulant effect; may cause hypertension when taken with thiazide diuretics (21,24,25)
Ginseng	Treatment of early menopause, menstrual disorders and digestive problems	Sleep and gastrointestinal disturbances; headaches; may decrease anticoagulant effect of warfarin and decrease plasma digoxin levels; may cause hypoglycemia (24,26,27)
Goldenseal	Treatment of infections and inflammation	Interactions with antihypertensive and anticoagulant medications; gastrointestinal discomfort (28,29)
Horse Chesnut	To reduce pain and inflammation associated with arthritis and rheumatism; cough remedy; fever reduction	Increased risk of bleeding with warfarin (24)
Noni	Immune system enhancement; aid to digestion	Hyperkalemia (30)
Saw Palmetto	Urinary tract ailments including prostatitis and benign prostatic hypertrophy	Minor gastrointestinal problems including nausea, vomiting, constipation and diarrhea; mild pruritis; headache; hypertension; erectile dysfunction (31)
St. John's Wort	Treatment of depression, infection, wounds and burns; relief from anxiety and sleeping disorders	Decreases blood levels of the cholesterol-lowering drug simvastatin; anticoagulant effects; interacts with the immunosuppressants cyclosporine and tacrolimus, increased risk of organ rejection (25,32,33)
Valerian Root	Relief from insomnia, anxiety and pain	Headache, dizziness, upset stomach (19)

tanical and any potential side effects and drug interactions. Most importantly, find a way to maintain an open line of communication and trust with your patients on the topic.

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