

Herbal nephropathy

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• گزارش مورد بیماری:

- آقای ۳۳ ساله مبتلا به دیابت تیپ ۱ از سال ۱۳۸۵ ، متاهل، بدون فرزند ، راننده کامیون ، بدون سابقه مصرف سیگار و مواد مخدر و با کمپلیانس بسیار پایین بعلت سندروم اورمی در مرداد ماه سال ۱۳۹۸ در بیمارستان بستری شده و بر روی همودیالیز قرار گرفته بیمار از سال ۱۳۹۶ فشار خون بالا داشته و سال ۱۳۹۸ رتینوپاتی دیابتی در وی گزارش گردیده
- در بررسی سوابق وی تا اردیبهشت ۱۳۹۸ تستهای عملکرد کلیه غیر طبیعی نبوده و پس از آن دچار افزایش تدریجی کراتینین سرم شده که سیر فزاینده داشته است به پزشک مراجعه کرده ولی بهبودی حاصل نشده.
- در سوابق دارویی از بهمن ماه ۱۳۹۷ بدنبال تبلیغات اثر داروی **گانودرما** بر بهبودی دیابت ، مصرف دارو را شروع کرده و تا زمان بستری وی ادامه داشته و بجز انسولین و داروی لوزارتان (به صورت نامرتب) داروی دیگری مصرف نمیکرده
- در سوابق قبلی وی هیچ اثری از بروز بیماری سیستمیک یا عفونی خاصی دیده نمیشود و تستهایی که در این زمینه انجام شده منفی بوده است .
- در سابقه فامیلی نکته خاصی دیده نمیشود اولین ویزیت وی در کلینیک سرپایی مهر ۱۳۹۸ بوده

Herbal Nephropathy

- Herbal medicines and supplements have enjoyed thousands of years of popularity
- One -fifth of US adults use an herbal product as part of their health care
- The reality is that adverse effects do exist, including those related to renal toxicity.

[Methodist DeBakey Cardiovasc J.](#) 2019 Jul-Sep; 15(3): 228–230.
doi: [10.14797/mdcj-15-3-228](#)

Herbal Nephropathy

[Amita Jain, MD](#) and [Juan Jose Olivero, MD](#)

Herbal Nephropathy

[Amita Jain, MD](#) and [Juan Jose Olivero, MD](#)

Multiple ways that herbal renal injury

1. Direct nephrotoxic effect of the compound or its metabolites
2. Toxicity of the additive compounds and adulterants used in manufacturing the product
3. The interaction of herbal agents with concomitantly administered drugs
4. Alterations in body homeostasis that result in nephrotoxic effect
 1. Excessive diuresis
 2. Rhabdomyolysis
 3. Nephrolithiasis

Incidence and prevalence of herbal nephropathy is not known



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**Use of Herbs Among Adults Based on Evidence-Based
Indications: Findings From the National Health Interview Survey**

Aditya Bardia, MD, MPH, Nicole L. Nisly, MD, M. Bridget Zimmerman, PhD, Brian M. Gryzlak, MSW, MA, and Robert B. Wallace, MD, MSc

From the Department of Epidemiology (A.B., B.M.G., R.B.W.), Department of Internal Medicine (N.L.N.), and Department of Biostatistics (M.B.Z.), University of Iowa, Iowa City.

Nephrotoxicity and Chinese Herbal Medicine

- According to the World Health Organization
 - Traditional medicine 75%–80% of the world population, mostly in the developing world
 - Mainstay of medical treatment
 - Complement treatment

Aristolochic acid nephropathy: a worldwide problem

Frédéric D Debelle ¹, Jean-Louis Vanherweghem, Joëlle L Nortier

DIRECT NEPHROTOXIC EFFECT

- Aristolochic acid (AA) nephropathy (زرآوند)
 - Chinese herbal weight-loss medications
 - The histopathology is consistent with tubular apoptosis and necrosis with significant interstitial fibrosis.
- Clinical presentation
 - Unexplained rise in creatinine
 - Profound anemia
 - Minimal proteinuria
 - Glycosuria
 - Sterile pyuria

Aristolochic acid

- Indications
 - Induce weight loss
 - Liver disease
 - Arthritis
 - Headache
 - Edema

Aristolochic acid nephropathy: a worldwide problem

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Clinical course

- Progression may occur in one of three ways
 - Complete resolution
 - AKI with subsequent slow progression (1-7 years) to ESRD
 - Chronic kidney disease with relatively faster progression (< 2 years) to ESRD.

Adulteration of Chinese herbal medicines with synthetic drugs: a systematic review

NEPHROTOXICITY FROM ADDITIVES AND ADULTERANTS

اضافه کردن (مواد ارزان تر یا نامرغوب یا مضر به مواد خوراکی)، بد افزایی کردن، در تولید
تقلب کردن، چیز تقلبی ساختن مثل ریختن اب در شیر

- Herbal medicine contained several undeclared pharmacological substances
- NSAID
- Heavy metal
 - Mercury
 - Arsenic (AKI with rhabdomyolysis)
 - Lead

Herb–drug interactions with St John's wort (*Hypericum perforatum*): an update on clinical observations

Francesca Borrelli ¹, Angelo A Izzo

TOXICITY FROM DRUG-HERB INTERACTIONS

- *Hypericum perforatum*, a medicinal herb known as St. John's wort
 - Help with symptoms of depression
- Activator of the cytochrome p450
- Lower serum levels of anti rejection medications
 - Risk of rejection
- Grapefruit and chamomile tea inhibit cyp450 enzymes
 - Increasing cyclosporine blood levels and the potential for serious systemic and renal toxicity

Table 1 Summary of interactions studies with St John's wort (*Hypericum perforatum* L.) pathway. The reported brand and daily dose of St John's wort (SJW) product

	Major relevant pathways	Sample size	SJW treatment (days)	Primary endpoint
CYP3A/P-glycoprotein substrates (ABCB1)				
Digoxin	PgP (ABCB1)	7	14	AUC
Digoxin	PgP (ABCB1)	7	14	AUC
Midazolam	CYP3A4	7	14	AUC
Midazolam	CYP3A4	20	14	AUC
Digoxin	PgP (ABCB1)	19	14	AUC
Ethinyl estradiol	CYP3A	16	14	AUC
Digoxin	PgP (ABCB1)	7	14	AUC
Ketodesogestrel	CYP3A4	16	14	AUC
Boceprevir	CYP3A4, PgP (ABCB1)	17	14	AUC
Digoxin	PgP (ABCB1)	7	14	AUC
Midazolam	CYP3A4	7	14	AUC
Fexofenadine	PgP (ABCB1), OATP1B3)	12	14	AUC

Understanding drug interactions with St John's wort (*Hypericum perforatum* L.): impact of hyperforin content

Other interaction

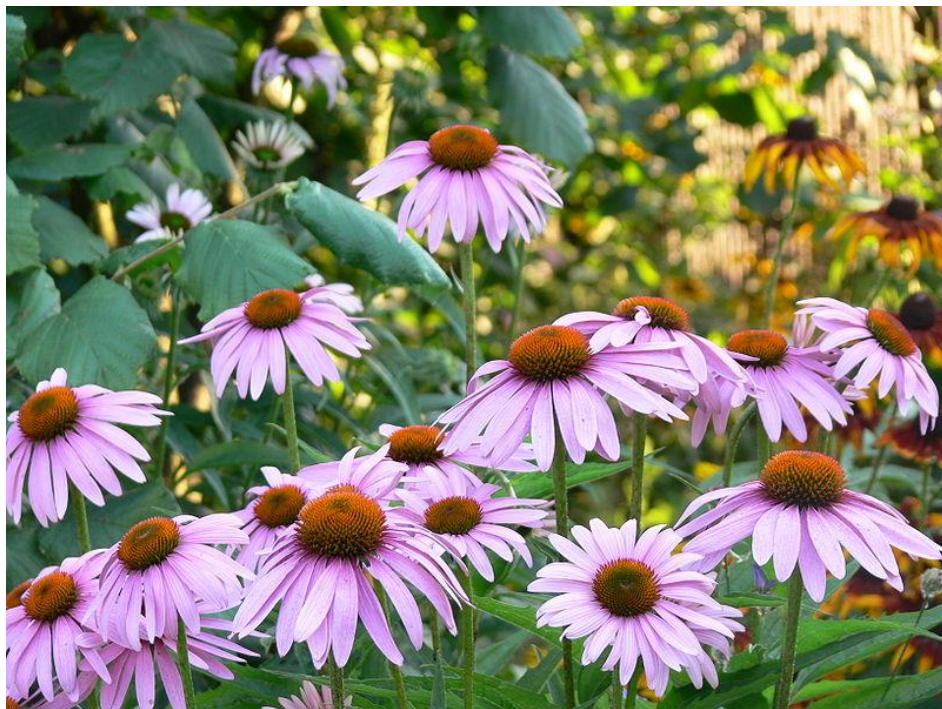
Dietary supplementation with cranberry concentrate tablets may increase the risk of nephrolithiasis

M K Terris ¹, M M Issa, J R Tacker

SUPPLEMENT-RELATED NEPHROLITHIASIS

- Cranberry supplements are very popular for prevention of recurrent UTI
- Excessive ingestion of cranberry products may result
 - Increased urinary excretion of calcium and oxalate
 - Calcium oxalate renal stones

سرخارگل (اکیناسه، اکیناشا) Echinacea



- یک گیاه دارویی است که استفاده آن در آمریکای شمالی و اروپا بسیار معمول است و به عنوان دارویی برای بهبود سرماخوردگی فروخته می‌شود.

- در ایران نیز این گیاه برای اولین بار در سال ۱۳۷۳ توسط زنده یاد مرحوم استاد رضا امیدبیگی در کشور کشت گردید و از آنجائیکه بومی ایران نبوده و فاقد نام فارسی بود، از اینرو مرحوم دکتر سید محمد فخر طباطبایی استاد دانشکده کشاورزی دانشگاه تهران نام "سرخارگل" را برای این گیاه برگزید.

Table 2. Chinese herbal medicines associated with nephrotoxicity

Possible Toxic Compound	Latin Name	English Name/ Chinese Name	Indications	Kidney Manifestations	Refs.
Aristolochic acid	<i>Aristolochia</i> spp.	Aristolochia, Guan Mu tong, Han Fang Ji	To induce weight loss, liver disease, arthritis, headache, edema	Chronic interstitial nephritis, renal interstitial fibrosis, Fanconi syndrome, urothelial carcinoma	19–22,43
Flavonoid (sciadopitysin)	<i>Taxus cerebica</i>	Chinese yew	Diabetes, vascular diseases	Acute tubular necrosis, acute interstitial nephritis	11
Flavonoid	<i>Cupressus funebris</i> Endl	Mourning cypress	Vascular diseases, instead of “yew”	Acute tubular necrosis, acute interstitial nephritis	14
Flavonoid oligomeric procyanthins	<i>Crataegus orientalis</i>	Hawthorn	Congestive heart failure, hypertension, hyperlipidemia	AKI	15
Ephedrine, norephedrine, pseudoephedrine	<i>Ephedra sinica</i>	Ma huang	Cough, to induce weight loss, to cause sexual arousal	AKI, nephrolithiasis	32–34,44
Glycyrrhetic acid, glycyrrhizic acid	<i>Glycyrrhiza glabra</i>	Licorice Gancao	Cough, sore throat, arthritis, to induce weight loss	Acute tubular necrosis, hypokalemic nephropathy, Fanconi syndrome	28–30,45
Anthraquinones, oxalic acid	<i>Rhizoma rhei</i>	Rhubarb	Laxative, anti- inflammatory	Interstitial fibrosis, tubular atrophy	31,45
Active moiety triptolide	<i>Tripterygium wifordii</i>	Lei Gong Teng	Arthritis, anti- inflammatory, immunomodulatory	Acute tubular necrosis	46

Typical toxic components in traditional Chinese medicine

Wen Lv, Jin-Hua Piao & Jian-Guo Jiang

Pages 985-1002 | Published online: 19 Sep 2012

Chinese Herbal Medicines Associated with Nephrotoxicity

- The main nephrotoxic components from herbs are aristolochic acids
- Derived from birthwort family of plants
 - *Aristolochia contorta* Bunge
 - *Aristolochia manshuriensis* Kom
 - *Clematis Chinensis* Osbeck
 - *Aristolochia cathcartii* Hook

Typical toxic components in traditional Chinese medicine

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- Nephrotoxicity
 - Anthraquinones
 - Flavonoids
 - Glycosides
- Carcinogenic
- Mutagenic
- Nephrotoxic

Manifestation of Nephrotoxicity Associated with Chinese Herbal Medicines

- Nephrotoxicity associated with Chinese herbal medicines includes:
- AKI
- CKD
- Nephrolithiasis
- Rhabdomyolysis
- Fanconi syndrome
- Urothelial Carcinoma

Acute renal failure by ingestion of *Euphorbia paralias*

Karima Boubaker ¹, Mondher Ounissi, Nozha Brahmi, Rym Goucha, Hafedh Hedri, Taieb Ben Abdellah, Fethi El Younsi, Hedi Ben Maiz, Adel Kheder

AKI

- *Euphorbia paralias* is known in traditional medicine as an anti-inflammatory agent, a purgative and for its local anesthetic property.
- The most common causes of AKI
 - Acute tubular necrosis
 - Acute interstitial nephritis

Andrographolide induced acute kidney injury: analysis of 26 cases reported in Chinese Literature

Wu-Xing Zhang ¹, Zhi-Min Zhang, Zhi-Qiang Zhang, Yang Wang, Wei Zhou

Andrographolide induced acute kidney injury:

- **analysis of 26 cases reported in Chinese Literature**
- Andrographolide paniculata, is widely used in China for the treatment of upper and lower respiratory tract infection, and dysentery etc
- Administered in 100-500 mL 5% glucose solution or normal saline
- AKI may occur shortly after intravenous infusion
 - Symptoms
 - Flank pain
 - Decreased urine output
 - Nausea or vomiting

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Chinese Herbal Medicine and CKD

- Vanherweghem and colleagues first described progressive chronic interstitial fibrosis and advanced kidney failure in nine young Belgian women who were using Chinese herbal slimming remedies.
- Aristolochic acid nephropathy (AAN)

Ma-huang strikes again: ephedrine nephrolithiasis

T Powell ¹, F F Hsu, J Turk, K Hruska

Nephrolithiasis

- There are two published patient reports of kidney stones associated with Ephedra sinica which is a very popular herb in treatment of respiratory conditions
- The components of the kidney stones
 - Ephedrine
 - Norephedrine
 - Pseudoephedrine



Review

Nephrotoxicity of Herbal Products in Europe—A Review of an Underestimated Problem

Katarzyna Kiliś-Pstrusińska ¹  and Anna Wiela-Hojeńska ^{2,*}

Mechanism of Plants Nephrotoxicity

- High relative proportion of blood flow through the kidneys
 - High metabolic activity
 - Glomerular filtrate reabsorption by the renal tubules
- Hemodynamic alterations
- Glomerular epithelial cell injury (podocytopathy)
- Renal inflammation

Prevention and Treatment

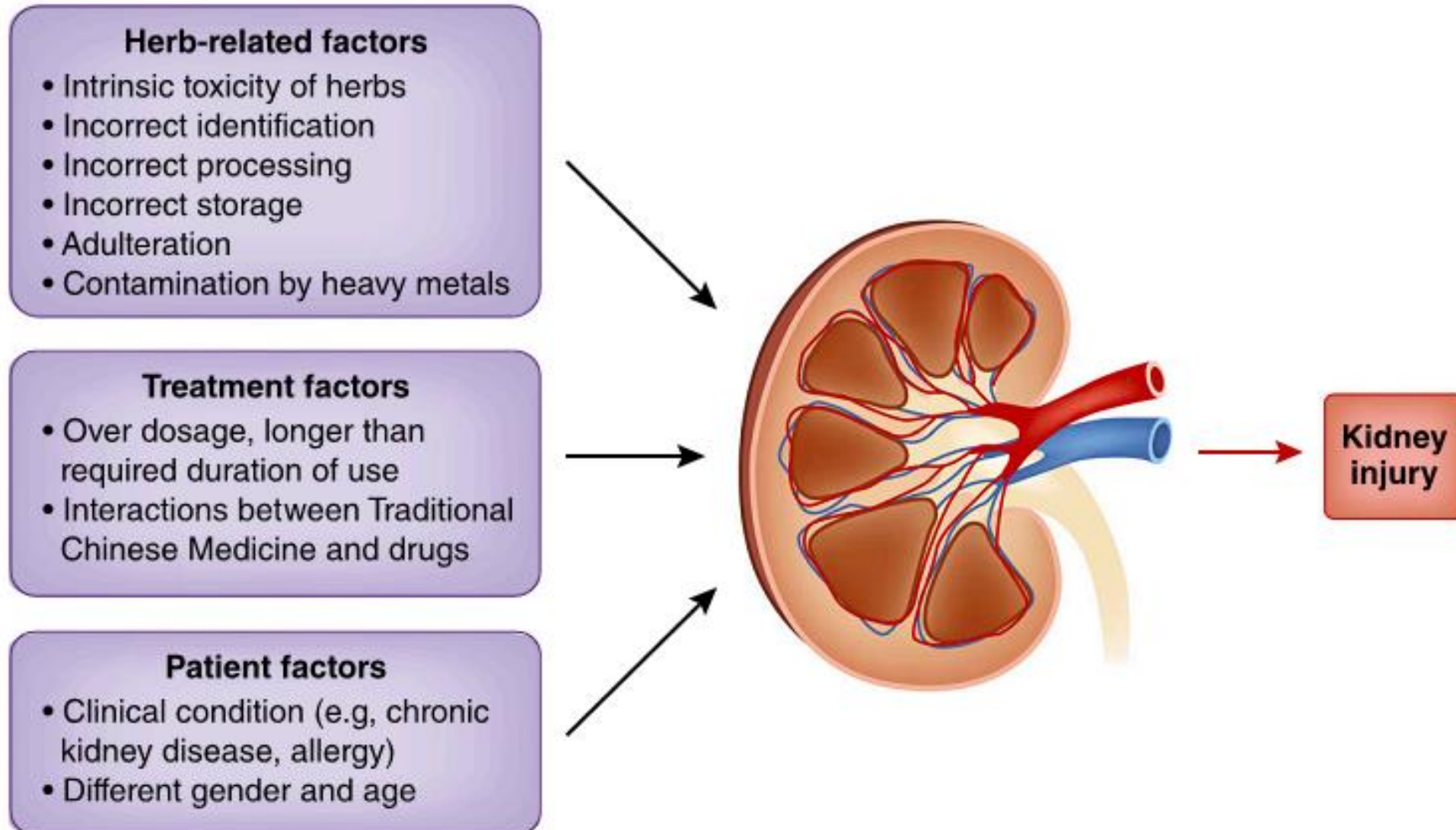
The first principle of effective therapy is prevention of toxicity

1. Avoid contamination with dangerous substances
2. Licensing of practitioners to ensure knowledge of traditional Chinese medicines and their potential side effects
3. Limitations on the dose and length of therapies as well as appropriate monitoring for adverse effects and
4. Development of a clear understanding regarding the potential interactions between herbal medicines and other medications

Methods to prevent nephrotoxicity associated with herbal medicine

- Increased attention should be given to the possible nephrotoxicity
- Preclinical pharmacologic and toxicologic assessment before widespread use
- Caution should be observed when using herbal associated with nephrotoxicity
- Avoid herbal medicine overdosage and long-term use
- Carefully record all cases of adverse reactions (e. g., kidney function, allergy)
- Develop a much stronger and more stringent system to manage toxicity in herbal medicine

Factors influencing the development of kidney disease associated with herbal medicine.





NATIONAL KIDNEY
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Herbal Supplements and Kidney Disease

Herbal Supplements and Kidney Disease

- **Is it safe to use herbal supplements if I have kidney disease?**
- Use of herbal supplements is often unsafe if you have kidney disease since some herbal products can cause harm to your kidneys and even make your kidney disease worse.
- Also, your kidneys cannot clear waste products that can build up in your body.

Herbal Supplements and Kidney Disease

- **What are the facts about herbal supplements?**
- FDA does not regulate herbal supplements for dose, content, or pureness.
- Some herbal supplements have aristolochic acid
- Herbal supplements made in other countries may have heavy metals.
- There are few studies to show benefits
- Herbal supplements may interact with prescription medicines

Herbal Supplements and Kidney Disease

- **Which herbal supplements have potassium?**
- Herbal supplements that have potassium include:

Alfalfa	American Ginseng	Bai Zhi (root)
بیترمه Bitter Melon (fruit, leaf)	Black Mustard (leaf)	Blessed Thistle
Chervit (leaf)	Chicory (leaf) گشنیز	Chinese Boxthorn (leaf) باکتورن
Coriander (leaf)	Dandelion (root, leaf)	Dulse
Evening Primrose	Feverfew	Garlic (leaf)
Genipap (fruit)	Goto Kola	Japanese Honeysuckle (flower)
Kelp	Kudzu (shoot)	Lemongrass
Mugwort	Noni	Papaya (leaf, fruit)
Purslane Sage (leaf)	Safflower (flower) گلرنگ	Sassafras
Scullcap	Shepherd's Purse	Stinging Nettle (leaf) گزنه
زردچوبه Turmeric (rhizome)	Water Lotus	

Herbal Supplements and Kidney Disease

- **Which herbal supplements have phosphorus?**

American Ginseng	Bitter Melon	Borage (leaf)
Buchu (leaf)	Coriander (leaf)	Evening Primrose
Feverfew	Flaxseed (seed)	Horseradish (root)
Indian Sorrel (seed)	Milk Thistle	Onion (leaf)
Pokeweed (shoot)	Purslane	Shepherd's Purse
Silk Cotton Tree (seed)	Stinging Nettle (leaf)	Sunflower (seed)
Turmeric (rhizome)	Water Lotus	Yellow Dock

Herbal Supplements and Kidney Disease



- **Which herbal supplements should I avoid if I have kidney disease?**

Astragalus

Barberry زرشک

Cat's Claw

Apium Graveolens

Creatine

Goldenrod

Horsetail

Huperzinea

Java Tea Leaf

Licorice Root

Nettle, Stinging Nettle گزنه

Oregon Grape Root

Parsley Root

Pennyroyal

Ruta Graveolens

Uva Ursi

Yohimbe

Herbal Supplements and Kidney Disease

- **What about herbal supplements that act like a "water pill"?**
- Some herbal supplements that act like a diuretic or "water pill" may cause "kidney irritation" or damage.
- These include bucha leaves and juniper berries.
- Uva Ursi and parsley capsules may also have bad side effects.

Herbal Supplements and Kidney Disease

- **Can herbal supplements interfere with the other medicines I take?**
- St. Johns Wort
- Echinacea
- Ginkgo
- Garlic
- Ginseng
- Ginger
- Blue cohosh
- There is interaction between herbal supplements and medicines could put you at risk for losing your kidney.

Herbal Supplements and Kidney Disease



- **Are there other health related issues for herbal supplements?**
- As with anyone, patients with kidney disease may have other health related issues
- Patients at high risk
 - History of a bleeding disorder
 - Women who are pregnant or lactating
 - Children

Herbal Supplements and Kidney Disease

- **What should I tell my doctor, dietitian or other healthcare provider?**

In general, it is not recommended for patients with kidney disease to use herbal supplements.

- If you choose to take one, always tell your doctor, dietitian, or other health care provider.

روزگارتان غرق در شادی

