

The Longwood Herbal Task Force
(<http://www.mcp.edu/herbal/default.htm>) and
The Center for Holistic Pediatric Education and Research
(<http://www.childrenshospital.org/holistic/>)

Uva ursi (*Arctostaphylos uva-ursi*)

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Principal Proposed Use: Treatment for mild, uncomplicated urinary tract infections (UTIs)

Other Proposed Uses: Prevention of UTIs; treatment of inflammatory conditions of the urinary tract, bladder spasms, renal stones, childhood enuresis, and urinary incontinence; diuretic; weight loss aid; topically as a skin lightening agent

Overview

Uva ursi has been used historically as an herbal remedy for mild cystitis, and is recommended by the European Scientific Cooperative on Phytotherapy as a treatment for uncomplicated cystitis that does not require antibiotics. There are data from *in vitro* studies and animal experiments that support this use. However, there are no randomized, controlled clinical trials evaluating its use in treating acute, symptomatic cystitis or pyelonephritis. There are no studies comparing it with standard antimicrobials for any serious infection. There are no scientific studies supporting its use as a treatment for childhood enuresis or adult renal stones, or for its use as a diuretic or to promote weight loss. Hydroquinone, the major metabolite of uva ursi, is used in a number of topical skin lightening medications, and there is good experimental support for this use. Due to its high tannin content, uva ursi may cause nausea and intestinal irritation acutely. Due to the documented hepatotoxicity, mutagenicity and carcinogenicity of hydroquinones in animal studies, it is only advised for intermittent, short-term use and is contraindicated during pregnancy, lactation and childhood.

Historical and Popular Uses

Uva ursi or bearberry has long been a part of North American and European herbal traditions as a remedy for urinary tract infections (UTIs), dysuria, kidney stones and chronic

cystitis^{1, 2}. Native Americans combined it with tobacco for smoking. Eastern Europeans used it to reduce maternal post-partum hemorrhage. It has been used topically and internally as an astringent treatment for dysentery and menorrhagia, and as an antiseptic for gonorrhea, vaginal ulceration, urethritis, and leukorrhea³. From 1820 to 1950, uva ursi leaf was listed on the US national formulary as a urinary antiseptic; it was a major therapy for UTIs prior to the introduction of antibiotics. Although it is no longer listed in the US pharmacopoeia, it is still recommended by the European Scientific Cooperative on Phytotherapy (ESCOP) as a treatment for uncomplicated cystitis in cases in which antibiotics are not required⁴⁻⁶. The German Commission E Monographs recommend it for inflammatory conditions of the lower urinary tract⁷. Some herbalists have advocated it for urinary spasms, mild incontinence, childhood enuresis and as a mild diuretic and weight loss agent⁸⁻¹⁰. Hydroquinones are also used topically as skin lightening agents.

Botany

Medicinal species: Arctostaphylos uva-ursi (L.) Sprengel, also known as *Arbutus uva ursi*

Common names: Arberry, bearberry, bear grape, hog berry, kinnikinnik, manzanita, mountain cranberry, mealberry, ptarmigan berry, rock berry, sand berry, whortle berry^{1, 2, 7}

Botanical family: Ericaceae (like blueberry and cranberry)

Plant description: Uva ursi is a low growing (20 inches tall) perennial shrub with creeping stems. It has small, dark, fleshy leaves; the flowers are bell shaped, white or pink. Its dull reddish orange berries are favorites of bears; hence its name: *uva* (grape) *ursi* (bears).

The leaves are the parts used medicinally¹. The berries are not used medicinally.

Where it's grown: Temperate, forested regions in the northern hemisphere

Biochemistry

Uva Ursi: Potentially Active Chemical Constituents

- Hydroquinones: arbutin, methylarbutin, hydroquinone¹¹
- Flavonoids: quercetin, kaempferol, myricetin glycosides¹²
- Tannins (20%): gallotannin and others^{13, 14}
- Triterpenes and phenolic acids, gallic acid, ursolic acid, malic acid, quinic acid^{3, 15, 16}

The leaves typically contain 5-15% *arbutin* and up to 4% *methylarbutin*¹⁷⁻¹⁹. The arbutin content varies over the growing season; leaves are often harvested in the fall^{16, 20}. Standardized products contain not less than 8% hydroquinones expressed as anhydrous arbutin (C₁₂H₁₆O₇). Arbutin is metabolized by intestinal bacteria to aglycone hydroquinone, which is absorbed, conjugated to glucuronides and sulfate esters in the liver and excreted renally^{5, 21, 22}. Arbutin is rapidly absorbed after oral administration; renal excretion is also rapid, and 75% is excreted within the first 24 hours^{5, 23}. Arbutin is also found in other herbs and foods, such as sweet marjoram²⁴, pears, wheat, coffee, tea and broccoli; consuming arbutin-containing foods results in significant increases in serum and urinary levels of hydroquinone and its metabolites, peaking at 12 times background levels within two to three hours following a meal²⁵.

Ursolic acid and *isoquercetin* have been reported to be mild diuretics^{1, 26}.

Uva ursi contains a higher percentage of *tannins* (20%) than almost any other herb. Tannins are typically used topically as astringents and internally to treat diarrhea; they may cause gastrointestinal irritation, and prolonged use may be hepatotoxic and carcinogenic¹⁴. Using cold water extraction (maceration) may reduce the amounts of tannins extracted and thus reduce toxicity²⁷.

Experimental Studies

Uva Ursi: Potential Clinical Benefits

1. Cardiovascular: none
2. Pulmonary: none
3. Renal and electrolyte balance: Diuretic and treatment for renal stones, incontinence and childhood enuresis
4. Gastrointestinal/hepatic: none
5. Neuro-psychiatric: none
6. Endocrine: Weight loss
7. Hematologic: none
8. Rheumatologic: none
9. Reproductive: none
10. Immune modulation: Anti-inflammatory
11. Antimicrobial: Antibacterial for prevention and treatment of UTI
12. Antineoplastic: none
13. Antioxidant: none
14. Skin and mucus membranes: Astringent; melanogenesis inhibition
15. Other/miscellaneous: none

1. **Cardiovascular:** none
2. **Pulmonary:** none
3. **Renal and electrolyte balance:** Diuretic and treatment for renal stones, incontinence and childhood enuresis. Uva ursi's historical use for these purposes has not been evaluated in any *in vitro*, animal or human studies^{16, 28}.
4. **Gastrointestinal/hepatic:** none
5. **Neuro-psychiatric:** none
6. **Endocrine:** Weight loss. Uva ursi's current promotion as a weight loss aid is based on its alleged effects as a diuretic; there are no *in vitro*, animal or human studies to support this use⁹.
7. **Hematologic:** none

8. **Rheumatologic:** none

9. **Reproductive:** none

10. **Immune modulation:** Anti-inflammatory

i. *In vitro data:* none

ii. *Animal data:* In the animal model of contact dermatitis (Type IV allergic reactions), arbutin synergistically enhanced the anti-inflammatory effect of prednisolone, dexamethasone and indomethacin in mice; arbutin alone had no anti-inflammatory activity at low doses (10 mg/ kg) and weak to moderate anti-inflammatory activity at higher doses (50 mg/kg)²⁹⁻³².

iii. *Humans:* There are no studies evaluating uva ursi's use as an anti-inflammatory agent in humans.

11. **Antimicrobial:** Antibacterial for prevention and treatment of UTI

i. *In vitro data:* Both the crude leaf extract and arbutin have demonstrated *in vitro* bacteriostatic activity against *Bacillus subtilis*, *E. coli*, *Enterobacter*, *Helicobacter pylori*, *Klebsiella*, *Shigella sonnei*, and *Shigella flexneri*³³⁻³⁵. Arbutin also repressed the expression of a key virulence factor for *Listeria monocytogenes*³⁶. Arbutin and its metabolites inhibited the growth of *Pseudomonas aeruginosa*, *Ureaplasma urealyticum* and *Mycoplasma hominis in vitro*^{37, 38}. The urine of adult volunteers who consumed arbutin or uva ursi tea was noted to be strongly antibacterial⁵. In another study, the urine of healthy volunteers given 100 milligram to 1 gram of arbutin showed similar activity as gentamicin and nalidixic acid against several uropathogens (*E. coli*, *Proteus mirabilis*, *Pseudomonas aeruginosa*)⁶. Activity was greatest in urine with the most alkaline pH.

ii. *Animal data:* Among white rats with experimentally induced pyelonephritis, doses of 25 mg/kg of uva ursi extract exhibited marked antibacterial and nephroprotective effects³⁹.

iii. *Human data:*

UTI prophylaxis: In a randomized controlled trial of 57 women who suffered from recurrent urinary tract infections, none of the 30 women randomized to uva ursi treatment for one month developed infections whereas five of the 27 assigned to placebo treatment did⁴⁰. There are no controlled trials comparing the safety and effectiveness of uva ursi to antimicrobials in preventing recurrent UTI in adults or children. There are no studies

evaluating uva ursi as an adjunctive therapy (along with antimicrobials) for UTI prophylaxis.

UTI treatment: German case series in adults given herbal mixtures including uva ursi tend to support its use in treating frequent and painful urination⁴¹. However, there are no randomized controlled clinical trials evaluating the effectiveness of uva ursi alone in treating acute cystitis or comparing it with standard antibiotics. Its use in treating subclinical infections, or patients who are symptomatic but whose urine cultures show less than 100,000 cfu/ml, has not been evaluated.

12. **Antineoplastic:** none

13. **Antioxidant:** none

14. **Skin and mucus membranes:** Astringent, melanogenesis inhibition

a. Astringent: This traditional use as an is reasonable based on uva ursi's tannin content, but has not been evaluated in any *in vitro*, animal or human studies.

b. Melanogenesis inhibition: Arbutin has been used to inhibit melanogenesis in treating hyperpigmented skin lesions such as chloasma^{42, 43}. Hydroquinone is the active ingredient in a number of non-prescription and prescription strength products used to decrease hyperpigmentation, such as Esoterica, Porcelana, Eldopaque Forte, Melpaque HP and others.

i. *In vitro data:* Cultured B16 melanoma cells treated with arbutin exhibited a significant, dose-dependent decrease in tyrosinase activity and melanin production⁴⁴⁻⁴⁸. In two studies of cultured human melanocytes, arbutin inhibited tyrosinase activity and melanin production^{49, 50}.

ii. *Animal data:* The melanogenesis of brown-haired guinea pigs was reduced 80% by topical application of arbutin⁵¹.

iii. *Human data:* In a pilot study of healthy adults who were exposed to ultraviolet B radiation and then treated with arbutin topically, there was an inhibition of hyperpigmentation in four of the six volunteers⁵².

15. **Other/miscellaneous:** none

Toxicity and Contraindications

All herbal products carry the potential for contamination with other herbal products, pesticides, herbicides, heavy metals, pharmaceuticals, etc.

This is particularly concerning with imports from developing countries.

Furthermore, allergic reactions can occur to any natural product in sensitive persons.

Potentially toxic compounds in uva ursi: Hydroquinones, tannins

Acute toxicity: Tannins may cause nausea, vomiting, diarrhea and intestinal irritation. Taking uva ursi with meals may minimize these effects. The oral LD50 of hydroquinone in 2% aqueous solution has been reported as 320 mg/kg in rats, 400 mg/kg in mice and 550 mg/kg in guinea pigs, 70 mg/kg in cats and 200 mg/kg in dogs^{1, 4}. There is one report of an adult who took 1 gram of uva ursi and experienced severe, acute toxicity: tinnitus, nausea, vomiting, cyanosis, seizures and collapse¹; another individual died after taking 5 grams of hydroquinone (equivalent to 30-100 grams of plant material)¹². On the other hand, doses of up to 20 grams of uva ursi have not resulted in serious toxicity in other healthy individuals⁵³.

Chronic toxicity: Hydroquinones are hepatotoxic, nephrotoxic, mutagenic and carcinogenic in animal studies⁵⁴⁻⁵⁶. In the standard Ames test, no genotoxic effects were observed in the urine of 12 adults given 420 milligrams of arbutin orally; only 0.6% of the administered dose was excreted as free hydroquinone in the urine, whereas 70% was excreted as conjugations of glucuronide or sulfate²². There appear to be differences between animals and humans in arbutin metabolism, making it much riskier for rats than for humans. In epidemiologic studies, workers exposed to high levels of hydroquinones actually had lower cancer rates and death rates than unexposed workers. Corneal and dermal damage has been reported in workers chronically exposed to hydroquinones, but there have not been any serious toxic effects noted in humans who take the kinds of doses recommended for medicinal purposes[DeCaprio, 1999 #117].

Limitations during other illnesses or in patients with specific organ dysfunction: Due to its tannin and hydroquinone content, uva ursi is not typically recommended for patients with severe renal or hepatic disease or gastrointestinal irritation^{57, 58}.

Interactions with other herbs or pharmaceuticals: Uva ursi appears to be most effective in an alkaline environment. Theoretically, medications and herbs that acidify the urine (e.g. Vitamin C or cranberry juice) may interfere with its activity⁴.

Safety during pregnancy, lactation and/or childhood: Due to its hydroquinone content, uva ursi is not recommended during pregnancy, lactation, or childhood. Some herbalists allege that uva ursi is oxytocic, but there are no scientific data supporting this claim; one study in guinea pigs showed that uva ursi had no effect on uterine tone⁵⁹.

Typical Dosages

Provision of dosage information does NOT constitute a recommendation or endorsement, but rather indicates the range of doses commonly used in herbal practice.

Doses are given for single herb use and must be adjusted when using herbs in combinations. Doses may also vary according to the type and severity of the condition treated and individual patient conditions.

Recommendations for optimal dosages of uva ursi vary among different herbalists.

Examples of adult dosages:

Standardized extract: 100-200 milligrams daily²

Arbutin: 400-800 milligrams daily divided into two to three doses⁶⁰

Maceration: 3-10 grams of dried herb daily^{16, 61, 62} prepared by maceration to reduce tannin extraction

Freeze dried leaves: 500-1,000 milligrams daily⁶⁰

Liquid extract (1:1 in 25% alcohol): 0.5-2.5 ml three to four times daily^{16, 28, 60}

Tincture (1:5 in 25% alcohol): 2-4 ml three to four times daily^{16, 60}

Treatment should be for no longer than seven to 14 days and should not be used more than five times a year to avoid toxicity¹⁶. Taking uva ursi with meals may reduce intestinal upset. An alkaline diet high in vegetables and fruit, and possibly supplemented with sodium bicarbonate, may enhance efficacy.

Availability of standardized preparations: Standardized products are available, particularly in Germany, but despite standardization, there is substantial variation in the amount of arbutin present in different preparations, and the amount may differ significantly from that stated on the label⁶³.

Dosages used in herbal combinations: Variable; often combined with buchu, cleavers, couchgrass, cowberry, cubeb, juniper berry, parsley, and/or yarrow¹⁰. No studies have evaluated the safety or effectiveness of these combinations.

Pediatric dosages: Unknown

Proprietary names: Arctuvan N, Cystinol Akut, Genocap, Uvalystat, Uva ursi capsules

Multi-ingredient preparations: Althaea complex, Buchu Compound, Cystinol, DeWitt's Pills, Premantaid, Tabritis, Urodil N, Urodil S, Uva-Ursi Plus, Uvacin, Waterlex,

See Also:

Uva Ursi Clinician Information Summary: <http://www.mcp.edu/herbal/uvaursi/uvaursi.cis.pdf>

Uva Ursi Patient Fact Sheet: <http://www.mcp.edu/herbal/uvaursi/uvaursi.ph.pdf>

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