Cat's Claw

Species (Family)

Uncaria tomentosa (Willd.) DC., *Uncaria guianensis* (Aubl.) Gmel. (Rubiaceae)

Synonym(s)

Life-giving Vine of Peru, Savéntaro, Uña de gato

Part(s) Used

Roots, root bark, stem bark and leaves

Pharmacopoeial and Other Monographs

None

Legal Category (Licensed Products)

Cat's claw is not included in the GSL.[G37]

Constituents

Alkaloids Both *U. tomentosa* and *U. guianensis* yield oxindole alkaloids, including isorhynchophylline and rhynchophylline and their *N*-oxides, mitraphylline and the indole alkaloids dihydrocorynantheine, hirsutine and hirsuteine.[1] *U. tomentosa* also contains isomitraphylline, its *N*-oxide, dihydrocorynantheine *N*-oxide and hirsutine *N*-oxide.[1]

There are two chemotypes of *U. tomentosa* which differ markedly in their patterns of alkaloids present in the root bark; in addition, the alkaloidal pattern of individual plants changes with time.[2,3] One chemotype primarily contains the pentacyclic oxindole alkaloids pteropodine, isopteropodine, mitraphylline, isomitraphylline, uncarine F and speciophylline,[4] whereas the other chemotype primarily contains the tetracyclic oxindole alkaloids rhynchophylline and isorhynchophylline.[1] Although a particular plant may contain either tetracyclic or pentacyclic oxindole alkaloids predominantly, both types of alkaloids can co-occur in the same plant.[3,5]

Other constituents Quinovic acid glycosides have been isolated from both species.[6–9] Polyhydroxylated triterpenes[10] and steroids (β-sitosterol, stigmasterol, campesterol)[11] occur in *U. tomentosa*. An unidentified South American species of *Uncaria* (presumably either *U. guianensis* or *U. tomentosa*) contains polyphenols ((−)-epicatechin and procyanidins).[4]

Food Use

Cat's claw is not used in foods.

Herbal Use[G32]

Cat's claw is stated to possess anti-inflammatory, antiviral, antioxidant, immunostimulating, antirheumatic and anticancer properties. It is native to the Amazon and has been used traditionally to treat gonorrhoea, dysentry, arthritis, rheumatism, gastric ulcers and various tumours.[12] It is also reputed to be a contraceptive.

Dosage

Commercial products (tablets, capsules) contain varying amounts of material, ranging from 25 to 300 mg standardised extract and from 400 mg to 5 g of plant material.[G31]

Pharmacological Actions

Several pharmacological activities have been documented for cat's claw, including anti-inflammatory, antimutagenic, antitumour, antioxidant and immunostimulating properties. The pharmacological activities of cat's claw have been reviewed.[12,13]

In vitro and animal studies

Certain oxindole alkaloids isolated from *U. tomentosa* (isopteropodine, pteropodine, isomitraphylline, isorhynchophylline) have been shown to enhance phagocytosis markedly *in vitro*.[14] Pentacyclic oxindole alkaloids from *U. tomentosa* have been reported to induce the release of a lymphocyte proliferation-regulating factor from human endothelial cells; tetracyclic oxindole alkaloids were found to reduce the activity of pentacyclic oxindole alkaloids on these cells in a dose-dependent manner.[12,15] Stem bark extracts of *U. tomentosa* have also been shown to stimulate interleukin 1 (IL-1) and interleukin 6 (IL-6) production *in vitro* in rat alveolar macrophages in a dose-dependent manner (range 0.025–0.1 mg/mL)

and to potentiate the production of IL-1 and IL-6 in lipopolysaccharide-stimulated macrophages.[16]

Extracts and fractions of *U. tomentosa* bark have shown no mutagenic effect but demonstrated a protective antimutagenic effect *in vitro* against 8-methoxypsoralen- and UVA-induced photomutagenesis in *Salmonella typhimurium* TA102.[17] It was suggested that this antimutagenic activity may be due to an antioxidant effect of *U. tomentosa*.[17]

In vitro antioxidant activity of stem bark and root extracts of *U. tomentosa* has been demonstrated in an assay using *tert*-butylhydroperoxide-initiated chemoluminescence in rat liver homogenates.[18] Extracts also prevented free radical-mediated DNA sugar damage.[18]

In vitro antitumour activity of water extracts of *U. tomentosa* (C-Med-100) has been shown in a human leukaemic cell line (HL-60) and a human Epstein–Barr virus (EBV)-transformed B lymphoma cell line (Raji).[19] The suppressive effect of *U. tomentosa* extracts on tumour cell growth appear to be mediated through induction of apoptosis.[19] The pentacyclic oxindole alkaloids uncarine C and uncarine E from *U. guianensis* have been identified as cytotoxic and DNA-damaging agents in a yeast-based assay.[20] These alkaloids also showed moderate cytotoxicity to several mammalian cell lines, including human lung carcinoma.[20] *In vitro*, aqueous extracts of *U. tomentosa* bark appear to interact with oestrogen receptor-binding sites.[21]

Rhynchophylline has been reported to inhibit rat[22] and rabbit platelet aggregation *ex vivo*.[23] Studies in cats and dogs have reported that rhynchophylline has a negative inotropic effect which can contribute to a hypotensive effect.[24] Rhynchophylline and isorhynchophylline have been reported to have negative chronotropic and inotropic effects in isolated guinea-pig atria.[25] Isorhynchophylline has been reported to have hypotensive effects in rats and dogs.[26]

Trichloromethane/methanol and aqueous extracts of cat's claw (*U. tomentosa*) bark have demonstrated anti-inflammatory activity in the rat paw carrageenan-induced oedema test; a quinovic acid glycoside was identified as one of the active principles.[8] An aqueous extract of cat's claw (*U. tomentosa*) bark was reported to protect against oxidant-induced stress *in vitro* and to attenuate indomethacin-induced chronic intestinal inflammation in rats.[27] Cat's claw extract was found to prevent the activation of the transcription factor NF-κB, which suggests a mechanism for the anti-inflammatory activity of cat's claw.[27]

Quinovic acid glycosides have demonstrated antiviral activity in *in vitro* tests against the RNA virus vesicular stomatitis virus.[7] Two quinovic acid glycosides also demonstrated *in vitro* activity against rhinovirus type 1B.[7]

Receptor-binding assays using dihydrocorynantheine isolated from the branchlet and hook of *Uncaria sinensis* (and also found in *U. tomentosa*) have shown that this alkaloid is a partial agonist for serotonin receptors.[28]

Clinical studies

There is a lack of clinical evidence to support the activities of cat's claw.

A decoction of *U. tomentosa* bark ingested daily for 15 days by a smoker decreased the mutagenicity induced in *S. typhimurium* TA98 and TA100 by the subject's urine; urine from a non-smoker who ingested the same regimen of *U. tomentosa* did not show any mutagenic activity before, during or after treatment.[17]

In an uncontrolled study, 13 HIV-positive individuals who refused to receive other therapies ingested 20 mg daily of an extract of *U. tomentosa* root (containing 12 mg total pentacyclic oxindole alkaloids per gram) for 2.2–5 months.[12] The total leukocyte number in the group was unchanged, compared with pretreatment values, whereas the relative and absolute lymphocyte count increased significantly. No significant changes in T4/T8 cell ratios were observed.[12]

Side-effects, Toxicity

There has been a report of acute renal failure in a Peruvian woman with systemic lupus erythematosus who had added a product containing cat's claw (one capsule four times daily, obtained from a local herbal shop) to her regimen of prednisone, atenolol, metolazone, frusemide and nifedipine.[29] The patient had a serum creatinine concentration of 3.6 mg/dL and was diagnosed with acute allergic interstitial nephritis. She was advised to discontinue cat's claw and, one month later, her renal function had improved (serum creatinine 2.7 mg/dL).

Data on the acute oral toxicity of *U. tomentosa* aqueous root extract (containing 35 mg total pentacyclic oxindole alkaloids per gram) in mice and four-week oral toxicity of an aqueous extract of *U. tomentosa* root (containing 7.5 mg total oxindole alkaloids per gram) in rats administered 1000 mg/kg/day have been summarised.[12] The acute median LD_{50} to mice was found to be greater than 16 g/kg body weight. In the study in rats, a slight but statistically significant increase in the percentage of lymphocytes and a decrease in the percentage of neutrophil granulocytes were seen. In addition, an

increase in the relative weight of the kidneys in rats of both sexes was noted, although kidney histology was normal.

In vitro, extracts of *U. tomentosa* have been shown to possess antitumour activity and to stimulate production of the cytokines IL-1 and IL-6, both of which are known to initiate a cascade of defence activities of the immune system. Oxindole alkaloids from *U. tomentosa* have been reported to enhance phagocytosis *in vitro* (*see In vitro* and animal studies).

The *in vitro* toxicity of aqueous extracts of *U. tomentosa* has been evaluated in bioassays using Chinese hamster ovary (CHO) cells and bacterial cells (*Photobacterium phosphoreum*).[30] At the concentrations used (10–100 mg/mL), the extracts did not show a significant cytotoxic effect in CHO cells and demonstrated a non-toxic effect in the bacterial cells used.

Contra-indications, Warnings

In view of its immunostimulant properties, cat's claw may interfere with immunosuppressive therapy. Extracts of the pentacyclic chemotype of *U. tomentosa* should be avoided where there is a risk of organ rejection in patients undergoing transplants; this includes bone marrow transplants.[13]

In view of the inhibitory effects of rhynchophylline on platelet aggregation,[22,23] it has been stated that cat's claw is contra-indicated in patients receiving anticoagulants and in those with coagulation disorders.[G31]

Animal studies have reported hypotensive effects with rhynchophylline[24] and isorhynchophylline;[26] thus, cat's claw should be used with caution in patients receiving antihypertensive agents.[G31]

Pregnancy and lactation The safety of cat's claw has not been established. In view of the lack of toxicity data, use of cat's claw during pregnancy and lactation should be avoided. In addition, use in children (<3 years) is not advised.

Pharmaceutical Comment

The chemistry of cat's claw is well documented. Reported pharmacological activities are mainly associated with the oxindole alkaloids and the quinovic acid glycosides.

The two species *U. tomentosa* and *U. guianensis* may be confused.[12] In addition, there are two chemotypes of *U. tomentosa*, one predominantly producing pentacyclic oxindole alkaloids, and the other tetracyclic oxindole alkaloids.[3,12] Since the tetracyclic oxindole alkaloids have been reported to antagonise the immunostimulant effect of the pentacyclic oxindole alkaloids on human cells *in vitro*,[12,15] it has been stated that mixtures of the two chemotypes of cat's claw are unsuitable for therapeutic use unless certified to contain less than 0.02% tetracyclic oxindole alkaloids.[31]

Documented scientific evidence from *in vitro* and, to a lesser extent, animal studies provides some supportive evidence for some of the uses of cat's claw. However, there is a lack of clinical data, and well-designed clinical trials involving adequate numbers of patients and using standardised preparations manufactured from the appropriate chemotype are necessary.

In view of the lack of toxicity and safety data, excessive use of cat's claw should be avoided. Individuals wishing to use cat's claw concurrently with conventional medicines should first seek advice from an appropriate healthcare professional.

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