

# CAT'S CLAW

## *Uncaria tomentosa* (Willd. ex Schult.) DC.

### *Family*

Rubiaceae: a family of flowering plants commonly known as the coffee or madder family. The two species *Uncaria tomentosa* and *Uncaria guianensis*, which is not as strong and is a common adulterant, may be confused although both have a long history of use by indigenous people.<sup>1</sup>

### *Parts Used*

Bark.

### *Description*

Cat's claw is a common, thick woody vine native to Peru, the Amazon rain forest and other tropical areas of South and Central America. It is described as a scrambling liana, which is a long-stemmed, woody vine that is rooted in the soil at ground level

and uses trees, as well as other means of vertical support, to climb up to the canopy to get access to well-lit areas of the forest. Cat's claw grows up to 20 to 30 meters long with the main stem growing up to 25cm in diameter. It grows as high as altitudes of 500 to 600 meters above sea level, in high forests with abundant sunshine and reaches 18 to 19 metres in height. The plant has hook-like thorns, growing largely along the vine in a leafy pattern, which resembles the claws of a cat. The plant is also known as the life-giving vine of Peru, *saventaro*, or *uña de gato*. The vernacular names cat's claw and *uña de gato* in Spanish may lead to confusion because they are used for at least 20 plants (from 12 families) with sharp, curved thorns. From the genus *Uncaria* the two most common species used and marketed interchangeably for their various properties are *Uncaria tomentosa* and *Uncaria guianensis*. *Uncaria tomentosa* is evidently



the preferred species partly because of its higher alkaloid content.<sup>2,3</sup>

### *Traditional Use*

Cat's claw has been used in traditional and cultural practices in South America for centuries, especially in Peru. Indigenous to Peru, the Ashaninka Indians classified it as a 'powerful plant' and used it to restore health. The Ashaninka's have used the root bark, and the stem bark as well, for generations. To the priests of this tribe cat's claw is a sacred plant used to eliminate disturbance in the communication between body and spirit. Traditionally it has been used in Peru in the form of aqueous or alcoholic infusions as an anti-inflammatory agent for arthritis, gastritis and other disturbances of the gastrointestinal system, for the treatment of cancer and for different skin disorders. It is also used for diabetes, asthma, diseases of the urinary tract, wounds and as a tonic to ward off disease. It has also been used as a contraceptive, emmenagogue and as abortifacient in premenstrual syndrome, menstrual irregularity and to recover from childbirth. One method of taking cat's claw is two spoonfuls of bark boiled in 1.5 litres of water for 30 minutes and left to cool. Half a glass of this liquid is taken three times a day before meals. Cat's claw has been used in Peru and Europe since the early 1990s as an adjunctive treatment for cancer and AIDS, as well as other diseases targeting the immunological system. Cat's claw was first described in 1830 and first studied in Peru by the German biologist Brell in 1950. Scientific studies with cat's claw began in the early 1970s when Austrian Klaus Keplinger organised the first work in the 1970s and 80s which led to several extracts of cat's claw being sold in Austria and Germany as well as four US patents describing extraction procedures for a group of chemicals, oxindole alkaloids and the immunostimulating actions of these alkaloids found in cat's claw. These novel oxindole alkaloids fuelled research and business worldwide. Cat's claw was traditionally used in massive concentrations as a contraceptive and in lower concentrations to dissolve tumours but not as an abortive. It is said that women in the Campa tribe boil six kilograms of the root in one litre of water, until it is reduced to about one cup. They filter it and drink the fluid during the menstrual

period for three consecutive months in order to avoid pregnancy for three or four years. It is said that to dissolve tumours the dosage is much less: 500g root in five litres of water for 30 minutes.<sup>4,5,6</sup>

### *Constituents*

Oxindole and indole alkaloids (pentacyclic and tetracyclic), pyroquinovic acid glycosides, organic acids, proanthocyanidins, flavonoids, sterols, polyoxygenated triterpenes, coumarins and tannins. While early studies focused on pentacyclic oxindole alkaloids as the primary active components, more recent studies report that activity is well spread over a range of polar constituents. One study suggests that the anti-inflammatory and antioxidant activities of cat's claw are not affected by the presence or relative level of alkaloids. About 50 different components have been isolated from cat's claw (considering all plant parts), 35 of which have been identified in only a couple of other species. Cat's claw occurs in two chemotypes that appear botanically identical, but are chemically different as each varies greatly in its alkaloid content. One predominantly contains pentacyclic oxindole alkaloids with little or no tetracyclic oxindole alkaloids while the other is rich in the tetracyclic oxindoles with either no pentacyclic oxindole alkaloids or a considerable amount of them. Tetracyclic oxindoles are considered antagonistic to the purported beneficial effects of the pentacyclic oxindole alkaloids and thus, the significance in distinguishing between the two chemotypes. Interestingly the native Ashaninka shamans of Peru are said to be able to identify the correct chemotype and they harvest only the chemotype containing mostly pentacyclic oxindole alkaloids. This is despite the fact that the two chemotypes are botanically identical (i.e. the plants look identical). Based on a 1998 preclinical study it has been stated that the mixture of the two chemotypes of cat's claw are unsuitable for therapeutic use unless certified to contain less than 0.02% tetracyclic oxindole alkaloids. Researchers suggest that these chemical constituents may be more useful as marker compounds rather than mediating the bioactivity of cat's claw.<sup>7,8,9,10,11,12,13</sup>

## Actions

Anti-inflammatory, antioxidant, antimutagenic, immunomodulatory, immunostimulant, antiviral, antibacterial, emmenagogue.

## Pharmacological Activity

The pharmacological data on cat's claw is diverse however of concern is that most of the studies indicate 'bark' for the drug used, without specifying whether it is root or stem. This monograph will focus on studies where stem bark is specified. Although there are no randomised controlled trials or published human outcome studies some conditions reportedly improved by cat's claw include osteoarthritis, rheumatoid arthritis, prostatitis, viral illnesses and cancer (acting as a non-specific immunomodulating agent) and it may also have potential as an immunomodulating adaptogen in cellular aging. The understanding of some specific mechanisms of molecular action leads to the demonstration of various anti-inflammatory, immunostimulating and protective effects.<sup>14</sup>

### Anticancer, Anti-inflammatory, Antioxidant and Antimutagenic Activity

A small preliminary study demonstrated relative safety and modest benefit of a cat's claw extract of the pentacyclic chemotype to the tender joint count in patients with active rheumatoid arthritis who were also taking pharmaceuticals as part of their treatment. Forty patients undergoing sulfasalazine or hydroxychloroquine treatment were enrolled in a randomised 52 week, two phase study. During the first phase (24 weeks, double blind, placebo controlled), patients were treated with cat's claw or placebo. In the second phase (28 weeks) all patients received the plant extract. Twenty-four weeks of treatment with the cat's claw extract resulted in a reduction of the number of painful joints compared to placebo. Patients receiving the cat's claw only during the second phase experienced a reduction in the number of painful and swollen joints.<sup>15</sup>

A controlled clinical trial with cat's claw suggests efficacy in the treatment of osteoarthritis of the knee. Forty-five patients with osteoarthritis of the knee were recruited, 30 were treated with commercially available purified freeze-dried extracts of cat's claw stem bark and 15 with placebo. Pain

associated with activity, medical and patient assessment scores were all significantly reduced, with benefits occurring within the first week of therapy. Cat's claw is an effective treatment for osteoarthritis due to its antioxidant and anti-inflammatory properties the study found. The anti-inflammatory action may result from its ability to inhibit TNFalpha and to a lesser extent PGE2 production.<sup>16</sup>

Since the late 1970s cat's claw, in different forms (e.g. extracts, tablets and capsules), has been introduced in Europe to treat patients suffering from cancer and some viral diseases. In addition to the anti-inflammatory properties of cat's claw its protective antimutagenic effects have also been demonstrated *in vitro* against photomutagenesis.<sup>17</sup>

Cat's claw decreased DNA damage (measured as single strand breaks in DNA) from single dose of hydrogen peroxide and increased DNA repair in a human volunteer study. A cat's claw nutraceutical had been shown to enhance DNA repair, mitogenic response and leukocyte recovery after chemotherapy-induced DNA damage *in vivo*. In the human volunteer study 12 apparently healthy adults working in the same environment were randomly assigned into three groups with age and gender matched. One group was daily supplemented with a 250mg tablet containing an aqueous extract of the cat's claw nutraceutical and another group with a 350mg tablet, for eight consecutive weeks.<sup>18</sup>

Some studies have shown that cat's claw can act as an antiapoptotic agent and enhance DNA repair in chemotherapy-treated cells although others have shown that it enhanced apoptosis. A 2017 *in vitro* study suggested that cat's claw could be useful in enhancing cell death following anticancer therapies including ionizing radiation. In this study the treatment of THP-1 monocyte-like cells with cat's claw increased their susceptibility to X-rays and the combination of cat's claw and X-ray exposure strongly inhibited cell signalling and promoted apoptosis.<sup>19</sup>

Preliminary chemical investigations of an aqueous cat's claw extract performed in 2017 revealed the presence of hydrophilic low-medium molecular weight metabolites with anticancer potential towards squamous carcinoma cells, precancerous and early forms of squamous cell carcinomas.

Squamous cell carcinoma (SCC) is an uncontrolled growth of abnormal cells arising in the skin's squamous layer of epidermis. When detected at an early stage SCCs are almost curable, however, if left untreated, they can penetrate the underlying tissue and become disfiguring. The study evaluated cell proliferation, apoptosis and the level of reactive oxygen species following cat's claw treatment. Cat's claw affected cell cycle progression and reduced cell viability in a dose and time-dependent manner.<sup>20</sup>

Antimutagenic *in vivo* tests showed that cat's claw displayed antimutagenic activities. The results of the 2017 study suggested a safe use of this herbal medicine that is available free of charge from the Brazilian Public Health System for the treatment of arthritis. Cat's claw could also effectively contribute to improving the quality of life and the recovery of people undergoing chemotherapeutical treatments.<sup>21</sup>

An *in vitro* study provides evidence for the widely held belief that cat's claw is an effective anti-inflammatory agent. The study found that an aqueous extract of cat's claw protects cells against oxidative stress and negated the activation of NF-kappaB. By preventing the activation of the transcriptional factor NF-kB cat's claw inhibits the expression of inducible genes associated with inflammation.<sup>22</sup> The results demonstrated that the aqueous extract of cat's claw elicited similar beneficial effects as an antioxidant which are consistent with previous findings using a bark methanol extract.<sup>23</sup> The primary mechanism for cat's claw anti-inflammatory actions appears to be immunomodulation via suppression of TNFalpha synthesis.<sup>24</sup>

### Female Health Activity

Cat's claw extract appears to be a promising alternative for treating endometriosis following a 2011 *in vivo* study. Experimental endometriosis was induced in twenty-five rats. After three weeks, 24 animals developed grade III experimental endometriosis and were divided into two groups. Group "U" received cat's claw extract orally (32mg/day) and group "C" (control group) received a 0.9% sodium chloride solution orally (1 mL/100g of body weight/day). At the surgical intervention, and after the animal was euthanised, the implant volume was calculated. The final average implant volumes

were significantly different between the groups. There was a significant increase between the initial and final average volumes in the control group, and treatment with the cat's claw caused a marked reduction in the growth over time.<sup>25</sup>

The findings of a 2011 study by the same Brazilian team suggests that cat's claw has a contraceptive effect. Once it was established that cat's claw reduces endometriosis experimentally the researchers wanted to evaluate the mechanism for the treatment of this pathology. Among the drugs commonly used to treat endometriosis are contraceptives with known action against endometriosis. In the evaluation of *in vitro* cultures of mammary tumour tissue (infiltrating ductal carcinoma, stage II and poorly differentiated) cat's claw was used and compared with methotrexate, where it was observed there was a decrease in specific areas of oestrogen receptors. Based on this premise the researchers conducted an *in vivo* study evaluating the histological changes in the parenchyma's epithelial layer of the uterus and ovaries of rats with induced endometriosis treated with cat's claw. Rats with experimental endometriosis were selected and divided in three groups: The cat's claw group received 32mg/mL of cat's claw extract, 1mL administered daily. On the 15th day of treatment the uterine horn and ovaries were removed for analysis and 90% of the cat's claw group had immature ovarian follicles whereas the placebo group did not present any changes.<sup>26</sup>

### Immunomodulatory, Immunostimulant and Antimicrobial Activity

Cat's claw enhanced response to pneumococcal vaccine by reducing decay of antibody titers and elevating lymphocyte/neutrophil a human intervention study found. Male volunteers were supplemented with a daily dose of 350mg x 2 of a nutraceutical extract of cat's claw for two months and compared with untreated controls for their abilities to respond to a 23 valent pneumococcal vaccine.<sup>27</sup>

While cat's claw's popularity is partly due to European reports of its clinical effectiveness in combination with AZT (zidovudine) for AIDS treatment these findings lack confirmation by well controlled clinical studies.<sup>28</sup>

An *in vivo* study found that cat's claw had a positive effect on myeloid progenitor numbers and is promising for use with chemotherapy to minimize the adverse effects of this treatment. Cat's claw has antioxidant activity and works as an agent to repair DNA damage. It causes different effects on cell proliferation depending on the cell type involved; specifically, it can stimulate the proliferation of myeloid progenitors and cause apoptosis of neoplastic cells. Neutropenia (low number of cells called neutrophils) is the most common collateral effect of chemotherapy predisposing patients to infection. For patients undergoing cancer treatment the administration of a drug that stimulates the proliferation of healthy hematopoietic tissue cells is desirable.<sup>29</sup>

*In vitro* studies demonstrate that a 95% ethanolic extract of cat's claw is able to elicit a response via an NF-kappaB-dependent mechanism.<sup>30</sup>

Treatment with cat's claw inhibits the production of the pro-inflammatory cytokine, TNF-alpha, which is a critical mediator of the immune response. An *in vitro* study showed that cat's claw inhibited the MAP kinase signalling pathway and altered cytokine expression.<sup>31</sup>

The results of an *in vitro* study suggest cat's claw has a strong immunostimulant action. Cat's claw greatly stimulated IL-1 and IL-6 production and were able to enhance IL-1 and -6 in stimulated macrophages.<sup>32</sup>

The data on the antiviral effects of cat's claw is very limited. Cat's claw has been used to treat viral diseases such as herpes but its therapeutic efficacy against this virus had not been investigated until recently. In an *in vitro* study the hydroalcoholic extracts of the stem bark exhibited antiherpetic activity (Herpes simplex virus type 1, HSV-1) by inhibiting the attachment of HSV-1. The antiherpetic activity from the samples under investigation seemed to be associated with the presence of polyphenols or their synergistic effect with oxindole alkaloids or quinovic acid glycosides, since both purified fractions did not present activity when evaluated alone. Inhibition of viral attachment in the host cells was the main mechanism of antiviral activity. Although both purified fractions displayed the lowest antimutagenic activity in pre and simultaneous treatment, they provided a similar

effect to that of cat's claw hydroethanolic extract in post-treatment. Given that purified fractions may result in a reduced antiherpetic activity, the use of cat's claw hydroethanolic extract from barks should be prioritised in order to obtain a synergistic effect.<sup>33</sup>

Cat's claw displayed immunomodulating and antiviral effects against dengue fever *in vitro*.

Several inflammatory mediators that are implicated in vascular permeability and shock are produced after dengue virus infection by monocytes, the primary targets for virus replication. A recent study assessed the immunoregulatory and antiviral activities from a 50% ethanolic extract of cat's claw which was tested in an *in vitro* dengue virus infection model. Cat's claw significantly decreased dengue virus monocytes.<sup>34</sup>

Cat's claw presented antimicrobial activity *in vitro* on *Enterobacteriaceae*, *Streptococcus mutans* and *Staphylococcus* spp. isolates.<sup>35</sup>

## Indications

- Rheumatism and as an adjunct therapy to conventional treatment (it helps reduce the number of painful and swollen joints), inflammation of the joints, arthritis (all kinds), muscle pains, strains and injuries
- Other inflammatory conditions such as cystitis, Crohn's, colitis, diverticulitis, irritable bowel syndrome (IBS), gastric ulcers, gastritis or other disturbances in the gastro-intestinal system
- For strengthening the immune system and as an adjuvant therapy in acute and recurrent infectious diseases particularly viral infections including human papilloma virus (HPV), herpes zoster, herpes simplex and human immunodeficiency virus (HIV) and dengue
- Adjunctive therapy for cancer (to reduce side effects of chemotherapy, radiation and protect cells)
- A general daily tonic (to tone, balance and strengthen all body functions), convalescence, debility, chronic fatigue syndrome and Lyme disease
- Externally for acute and chronic skin inflammation, such as cuts, bruises, burns or insect bites
- Reputed to be contraceptive

### *Energetics*

Warming.

### *Use in Pregnancy*

Owing to its traditional use as an emmenagogue and as a contraceptive at high dose its use during pregnancy and lactation is not recommended.<sup>36</sup>

### *Contraindications*

Based on the belief that cat's claw is an immunostimulant it is not advised for patients awaiting bone marrow or organ transplant, persons with medically-induced immunosuppression (e.g., patients with organ transplants), autoimmune disease, multiple sclerosis or tuberculosis. However, some researchers disagree with this view and suggest that cat's claw may be helpful for transplant patients.<sup>37</sup>

### *Drug Interactions*

Caution with protease inhibitors (e.g. antiviral drugs such as atazanavir, ritonavir, saquinavir) and anticoagulant/antiplatelet (such as warfarin) and immunosuppressant drugs.

### *Administration and Dosage*

Liquid Extract:	1:1
Alcohol:	60%
Weekly Dosage: <sup>38</sup>	15 to 40mL

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