

# Plant Profile, Phytochemistry and Pharmacology of Cat'claw Plant (*Uncaria Tomentosa*): A review

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## Abstract:

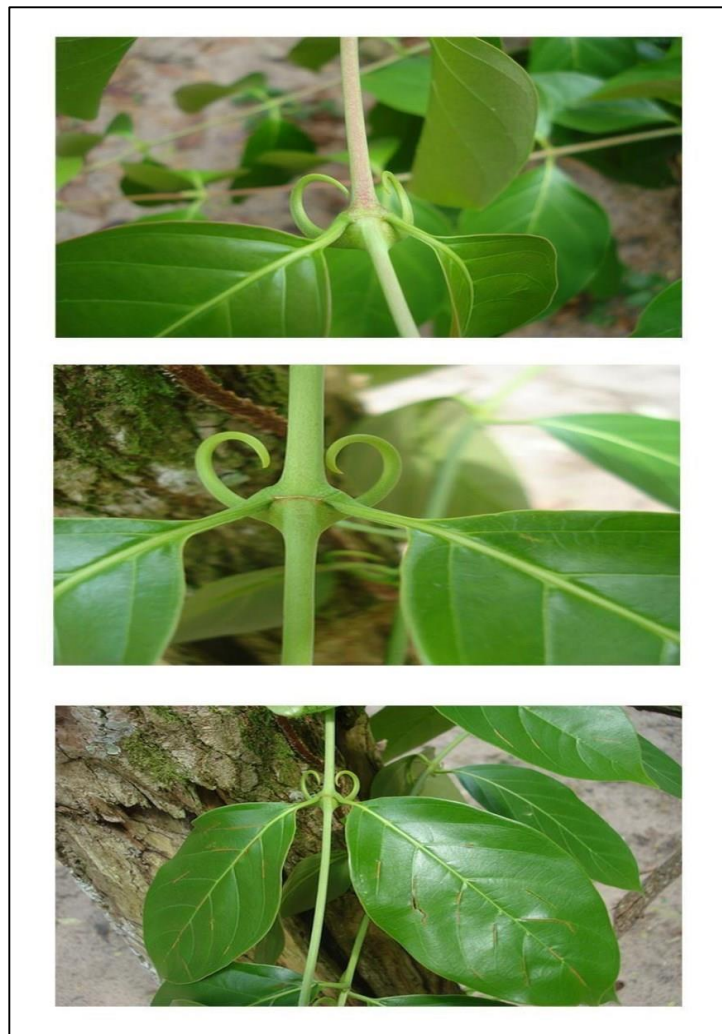
The tropical medicinal vine *uncaria tomentosa*, also referred to as cat's claw, is native to the Amazon rainforest and other regions of South and Central America. It has been proven to be useful as an immune system rejuvenator, antioxidant, antibacterial, and anti-inflammatory agent. Traditionally, it has been used to treat wounds, fever, urinary tract infections, viral infections, and asthma. Numerous phytoconstituents, including proanthocyanidins, sterols, organic acids, glycosides, oxindole and indole alkaloids, and triterpenes, are abundant in *U. tomentosa*. Theileria, Babesia, Plasmodium, and viruses are among the pathogenic bacteria, viruses, and microorganisms against which the biological activities of *U. tomentosa* have been studied.

Keywords: *Unacaria Tomentosa*; Cat's Claw; Biological Activities.

## 1. Introduction:

*Uncaria tomentosa* also known as "cat's claw," is a plant indigenous to the Amazon rain forest. Its hook-like thorns resembling a cat's claw have been used as traditional medicine in South American countries for its purported anti-inflammatory, immunomodulatory, and immunostimulant properties [1] its use has been investigated for anti-cancer [2] antiarthritic [3] and even mouse models of acute ischemic injury [4]. As a result, it can be found in several over-the-counter supplements worldwide. Despite their widespread availability, safety data are lacking, and their effects on the kidney are not well known. Acute interstitial nephritis (AIN) is a cellular inflammatory process of the kidney interstitium causing kidney dysfunction.

AIN can occur in the setting of an offending medication/ agent, infection, or autoimmunity Urinary sediment. A large proportion of the population living in developing countries in Asia and Africa depend on plant-based traditional medicines for primary care [5]. Plants are widely used because to their affordability and accessibility [6-8] acute interstitial nephritis (AIN) is a cellular inflammatory process of the kidney interstitium causing kidney dysfunction. AIN can occur in the setting of an offending medication/ agent, infection, or autoimmunity. Urinary sediment may show white blood cells (WBCs), WBC casts, and rarely micro-hematuria [9] On kidney biopsy, light microscopy findings include a cellular infiltrate of the interstitium accompanied by tubulitis and rarely eosinophils or plasma cells [10] We present a case of a patient who was on a strict ketogenic diet, utilizing over-the-counter diet shakes containing the herbal supplement *Uncaria tomentosa* who developed acute kidney injury (AKI) and was found to have biopsy-proven AIN. Stopping the keto-diet shake containing *Uncaria tomentosa* and concomitant corticosteroid therapy resulted in improvement in kidney function to near baseline[11].



**Figure 1:** Cat's claw plant (*Uncaria tomentosa*)

## 2. Chemical constituents of *u. tomentosa*:

*U. tomentosa* leaves contain higher oxindole alkaloid content than that present in stem bark and branches. This result is compatible with a study previously described by Laus et al. [12], who documented the accumulation of speciophylline and uncarine F (the main oxindole alkaloids) in leaves that can occur as tetracyclic oxindole alkaloid (TOA) or pentacyclic oxindole alkaloid (POA) derivatives. Both TOA and POA are liable to isomerization that depends mainly on medium polarity, pH, and temperature [13].

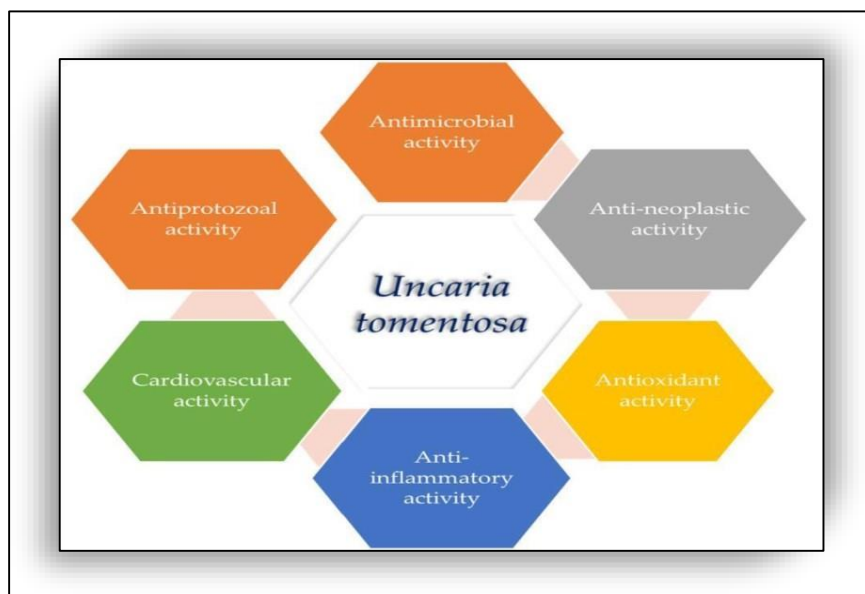
A recent study about the chemical variation of a wild population of cat's claw from Peru reported the existence of three specific chemotypes that producing different alkaloidal constituents [14]. Chemotype I is mainly composed of the POA with the intersection of D/E ring, chemotype II consists primarily of POA with trans D/E ring junction, while chemotype III consists primarily of TOA derivative unacrine C and E are two POA stereoisomers, while mitraphylline, rhynchophylline, and isorhynchophylline are TOAs found in cat's claw. On the basis of these results, the U.S. Pharmacopeia revealed that dried raw material of cat's claw included 0.05% (w/w) of the TOA concerning the POA amount, whereas cat's claw powdered dried extract, tablets, and capsules contained up to 25% (w/w). Cat's claw contains several active compositions including ajmalicine, campesterol, carboxyl alkyl esters, akuammigine, sitosterols, rutin, chlorogenic acid, speciophylline, catechin, cinchonain [15], corynoxine, harman, daucosterol, epicatechin, hirsutine, corynantheine, hirsutine, loganic acid, mitraphylline, iso-pteropodine, oleanolic acid, ursolic acid, lyaloside [16], rhynchophylline, palmitoleic acid, pteropodine quinovic acid glycosides, procyanidins stigmaterol, 3,4-dehydro-5-carboxystrictosidine, vaccenic acid, uncarine A thru F, and strictosidines [17]. Moreover, other reports revealed that various compounds other than oxindole alkaloids such as rotundifoline and isorotundifolone, coumarins, flavonoids, quinovic acid glycosides, and triterpenes may be responsible for the cat's claw medicinal effects [18].

## 3. Biological Activities of *U.tomentosa* Extract and Compound:

### 3.1 Tradational Uses:

In tropical South America, *U. tomentosa* bark and root have long been used as a remedy for a wide range of ailments, including infections, cancer, gastric ulcers, arthritis, and inflammations. Additionally it has been reported to be used for blood purifications, as a wound wash following childbirth to promote skin healing, kidney cleansing, asthma, inhibition of multiple diseases, irregular menstruation and hemorrhages, fevers, and to have a normalizing effect on bodily systems.

Additionally, it was used to cure a number of illnesses, such as weakness, rheumatism, urinary tract infections, abscesses, and contraception. It was also employed as a mental health therapy option (e.g., anxiety). [18,19].



**Figure 2.** Schematic representation of different pharmacological activities of *Uncaria tomentosa* (cat's claw).

### 3.2 Antioxidant Activity:

*U. tomentosa* contains alkaloids, flavan-3-ol monomers, and polyphenols, which contribute to its antioxidant properties. The preclinical examination found that the cat's claw protects against oxidative stress including peroxynitrite, which is associated with arthritis.

High doses of nonsteroidal anti-inflammatory medicines (NSAIDs) can block acute or chronic gastritis, as well as other chronic inflammatory illnesses [20, 21].

*U. tomentosa* aqueous extract has been shown to protect human erythrocytes from oxidative stress and alleviate chronic intestinal inflammation produced by indomethacin in rats [22, 23]. A study found that the cat's claw contains hydroxybenzoic acids, proanthocyanidins, and hydroxycinnamic acids, which contribute to its anti-inflammatory and radical scavenging properties [24, 25]. In an in vitro experiment, *U. tomentosa* bark demonstrated high antioxidant efficacy, as measured by trolox equivalent [26,27].

### 3.3 Anti-Neoplastic Activity:

Cat's claw was supposed to have antitumor and immunostimulatory effects because of its oxindole alkaloids content [23,28]. *U. tomentosa* extracts were found to have antiproliferative efficacy against SW620 colon adenocarcinoma, MCF7 breast cancer, and AGS gastric cells [19]. Interestingly, several studies suggested the antiproliferative effect of *U. tomentosa* against several cancer cell lines, namely cervical carcinoma, osteosarcoma, and breast cancer. For instance, an in vitro study reported that *U. tomentosa* hot water extract prevents inflammatory responses as well as tumor cell proliferation by inhibiting the transcriptional regulator nuclear factor kappa beta (NF-κB) activation without interfering with interleukin-2 (IL-2) production or IL-2 receptor signaling [29]. Cheng et al. [30] documented the antiproliferative effect of cat's claw extracts against several cell lines, including glioma, premyelocytic leukemia, MCF7.

### 3.4 Anti-Inflammatory Activity:

POA from *U. tomentosa* extract has been shown to enhance the lymphocyte proliferation-regulating factor produced from human endothelium cells. However, TOA has been reported to inhibit POA action on these cells in a dose-dependent manner [31-32]. Also, *U. tomentosa* stem.

Bark extracts promote IL-6 and IL-1 production in rat alveolar and lipopolysaccharide-stimulated macrophages, and decrease cancer cell multiplication through apoptosis induction [33,34,35]. Xiao et al. [33] studied the hypotensive effects of isorhynchophylline in rats and dogs, whereas Xiang et al. [36,37,38] found that rhynchophylline can reduce platelet buildup in rabbits and rat [40,41].

### 3.5 Antimicrobial, Antiprotozoal, and Antiviral Activities:

A prior study found that *U. tomentosa* bark extracts have antibacterial properties against *Borrelia burgdorferi* and respiratory infections such as *Enterococcus faecalis*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. The action was linked to the presence of Proanthocyanidins include dimers, oligomers, and undecamers.[42] *U. tomentosa* demonstrated significant antifungal activity against anidulafungin, terbinafine, and fluconazole-resistant nonalbicans species.[43] The reported antiprotozoal action against

*Babesia* and *Theileria* parasites, which was related to the ability to digest dangerous microbes. In addition, it has been shown to treat numerous parasites with the exception of *Giardia*. Therefore, *U. tomentosa* may be a suitable supplementary antiprotozoal herb.[44] Quinovic acid glycosides have been shown to have antiviral activity in vitro against vesicular stomatitis, ribonucleic acid (RNA), minus-strand RNA virus, and rhinovirus.[45] The study found that alkaloids and quinovic acid glycosides can protect against HSV infections and UV-induced DNA damage.[46]

### 3.6 Immunomodulatory Activity:

In vitro, the POA extracted from *U. tomentosa* extracts stimulated the immune system, whereas the TOA reduced it. In vitro studies found that cat's claw extracts and alkaloids can modulate immunobiochemical pathways that are increased by interferon-gamma.[47] In vivo research showed that *U. tomentosa* extracts had indirect immunomodulatory effect and increased myeloid progenitors in bone marrow by releasing physiologically active cytokines such as CSFs, IL-6, and IL-1. *U. tomentosa* extracts inhibited the MAPK signaling pathway and altered cytokine production in a human acute monocytic leukemia cell line. THP-1t [48].

### 3.7 Cardiovascular Activity:

*U. tomentosa* extracts inhibited the MAPK signaling pathway and altered cytokine production in a human acute monocytic leukemia cell line. THP-1t Hirsutine from *U. rhynchophylla* extract reduces intracellular calcium levels in rat aortas via blocking calcium channels and affecting calcium storage [49]. *U. tomentosa* extracts inhibited the MAPK signaling pathway and altered cytokine production in a human acute monocytic

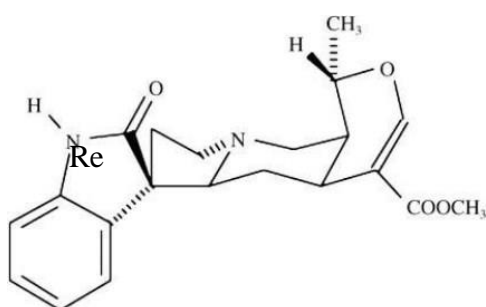
leukemia cell line. THP1t Furthermore, it has a vasodilating, negative chronotropic, and antiarrhythmic action. TOAs, including corynoxine, isocorynoxine, rhynchophylline, and isorhynchophylline, block  $Ca^{2+}$  channels, causing low blood pressure and potentially affecting the central nervous system.[50].

### 3.8 Anti-Alzheimer's Disease (AD) Activity:

*U. tomentosa* extracts inhibited the MAPK signaling pathway and altered cytokine production in a human acute monocytic leukemia cell line. THP-1t *U. tomentosa* has been shown to effectively remove  $A\beta$  plaques, making it a promising plant for Alzheimer's disease treatment. *U. tomentosa*'s polyphenolic components, specifically proanthocyanidins, have been found to reduce and inhibit plaque and tangle formation.

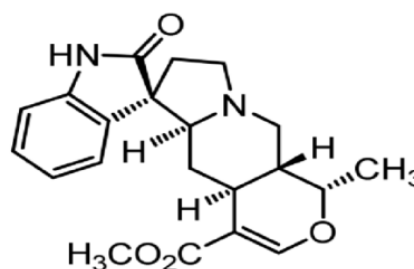
Proanthocyanidin B2 (epicatechin-4 $\beta$ -8-epicatechin) is a polyphenol that reduces brain plaque load and improves short-term memory in APP transgenic mice. Proanthocyanidin B2 inhibits brain inflammation, resulting in decreased astrocytosis and gliosis in TAD-41 transgenic mice [51].

#### List of some of bioactive alkaloids isolated from *Uncaria tomentosa*.

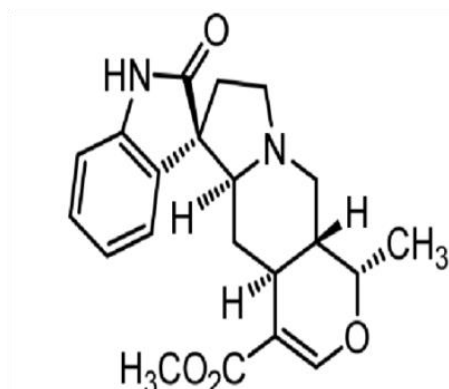


**Pteropodine**

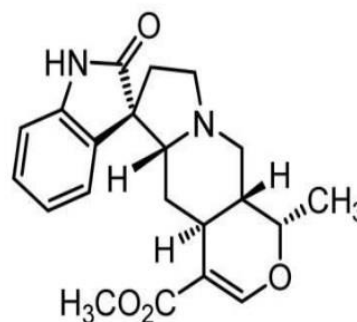
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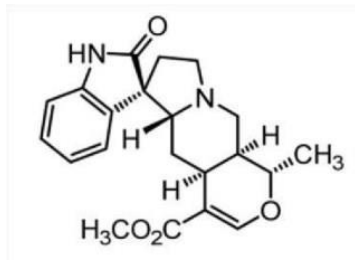
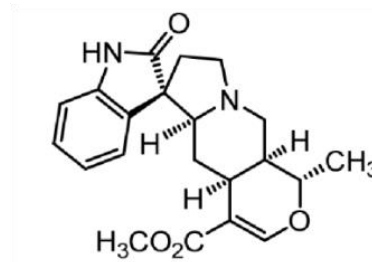
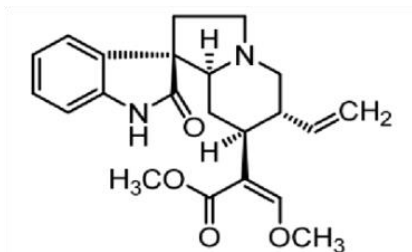
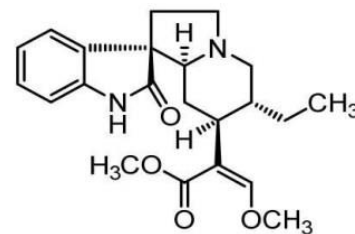
**Speciophylline**



**Mitraphylline**



**Isomitraphylline**

**Unacarine F****Isopteropidine****Corynoxine****Rhynchophylline**

#### 4. Reported Side Effect:

The American Herbal Products Association (AHPA) assigned cat's claw a class-4 safety rating, despite its traditional safety and non-toxicity, signifying a lack of scientific basis for herb safety evaluation]. High doses of cat's claw have been linked to undesirable effects such as nausea, acute renal failure, slow heart rate, stomach pain, hormonal effects, diarrhea, hepatotoxicity, low progesterone and estrogen levels, and neuropathy[52,53] Cat's claw may increase the risk of bleeding when combined with blood thinners like warfarin. Patients may be advised to discontinue its use before procedures [54,55].

Acute renal failure was reported in systemic lupus erythematosus patients after taking four capsules of cat's claw daily.

## **5. Precautions:**

### **5.1 Drug -Drug Interaction:**

#### **5.1.1 Immunosuppressant Drugs:**

POA isolated from cat's claw is believed to have an immunostimulatory effect and should not be used with immunosuppressant drugs such as cyclosporine, azathioprine, daclizumab, basiliximab, mycophenolate, muromonab-CD3, tacrolimus, sirolimus, corticosteroids, prednisone, or other chemotherapeutic drugs for autoimmune disease treatment or after organ transplantation [56].

#### **5.1.2 Anticoagulants:**

Cat's claw contains TOA, which increases the risk of bleeding when combined with aspirin, anticoagulant drugs like warfarin or heparin, NSAIDs like ibuprofen and naproxen, and antiplatelet drugs like clopidogrel. Due to rhynchophylline's inhibitory effect on platelet aggregation, patients may be advised to discontinue cat's claw administration before surgeries [55].

#### **5.1.3 Diuretic:**

Cat's claw, which has a diuretic effect, should not be combined with other diuretics as they share the same mechanism and may cause electrolyte imbalances. Furthermore, it may interact with hormonal, cholesterol-lowering, and kidney-related medicines [57].

#### **5.1.4 Antihypertensive Drug:**

Hirsutine extracted from cat's claw has hypotensive effects and should not be used by hypotensive individuals or those taking antihypertensive medications (e.g., casein protein, coenzyme Q-10 (ubiquinone), fish oil, L-arginine, Lycium, or stinging nettle). This is due to the hypotensive effects of rhynchophylline and isorhynchophylline, which can cause blood pressure to drop too low[33].

#### **5.1.5 Cytochrome P450 Substrates:**

Cat's claw inhibits microsomal CYP 3A4 activity, leading to higher serum levels of CYP 3A4metabolized medicines such nonnucleoside reverse transcriptase inhibitors, cyclosporine, and certain benzodiazepines, which can have substantial side effects [58]. The cat's claw may interact with various medications, including fexofenadine, paclitaxel, ketoconazole, antivirals, and oral contraceptives [59].

### **5.2 Drug Safety:**

*U. tomentosa* extracts appear safe when provided to treat inflammation, according to available data. Cat's claw safety has not been reported in breastfeeding and pregnant women, or children under the age of three, due to a lack of safety study [60].



## 6. Recommended Doses:

The average and recommended dose of *U. tomentosa* is one gram administered two to three times per day. Several clinical trials have employed a standardized extract of this species' chemotype, which contains less than 0.5% oxindole alkaloids and 8% to 10% carboxy alkyl esters, at dosages of 250 to 300 mg [68,69]. The average fatal dosage for a single dose of water extract from *U. tomentosa* in rats exceeds 8 g/kg. In humans, no toxic effects were observed after administering 350 mg/day for six consecutive weeks [18,70,71]. Cat's claw has recently been used to make tinctures, decoctions, capsules, extracts, and teas. For example, 250-1000 mg.

## 7. Conclusions:

This review examines the therapeutic properties and phytochemical compounds isolated from *U. tomentosa*. *U. tomentosa* (cat's claw) is used in traditional medicine to treat various health issues such as immune system deficiencies, neurodegenerative disorders, cancer, chronic fatigue syndrome, Crohn's disease, digestive complaints, parasitic and microbial infections, kidney cleanser, inflammatory problems, and irritable and leaky bowel syndrome. Furthermore, *U. tomentosa* contains numerous phytochemical compounds that are linked to its medicinal properties and exist in varying degrees in the herb. *U. tomentosa*, a natural herbal extract, effectively eliminates A $\beta$  protein "plaques". As a result, *U. tomentosa* may be a useful plant for treating Alzheimer's disease. Despite its medical benefits, cat's claw has various negative effects, including nausea, acute renal failure, stomach discomfort, and hormonal

## Abbreviations:

HIV	human immunodeficiency viruses
TOA	tetracyclic oxindole alkaloid
POA	pentacyclic oxindole alkaloid
IUPAC	International Union of Pure and Applied Chemistry
NSAID	nonsteroidal anti-inflammatory drugs TBARs
RNA	ribonucleic acid
HSV	herpes simplex virus
MAPK	mitogen-activated protein kinases
AD	Alzheimer's disease
A $\beta$	beta-amyloid

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