DOI: 10.18605/2175-7275/cereus.v12n2p119-129

ARTIGO DE REVISÃO

<< Recebido em 04/06/2019 Aceito em 16/05/2020. >>

REVISTA CEREUS ISSN: 2175-7275

Anti-inflammatory and diuretic activity of *uncária tomentosa* (cat's claw): systematic review

Larissa Jorge Coelho[1], Guilherme Nobre Lima do Nascimento[2]

RESUMO

O objetivo deste trabalho foi revisar a literatura sobre estudos que avaliam a atividade anti-inflamatória e diurética de *Uncaria tomentosa* (Willd. DC.), conhecida popularmente como unha de gato. Foi realizada uma pesquisa de artigos científicos de setembro a agosto de 2017, utilizando os descritores: *Uncaria tomentosa*, unha de gato, diuréticos e antiinflamatórios, como estratégias de busca. Estudos pré-clínicos *in vivo* e ensaios clínicos foram incluídos na avaliação da atividade anti-inflamatória e diurética de U. tomentosa. Dos 165 artigos encontrados, 10 estão de acordo com os critérios de inclusão, 50% (n = 05) com desenho experimental na forma de testes pré-clínicos in vivo, os ensaios clínicos corresponderam a um total de 30% (n = 03) e a amostra dos ensaios pré-clínicos in vivo e in vitro foi equivalente a um total de 20% (n = 02). As propriedades mais estudadas de U. tomentosa são anti-inflamatórias, antioxidantes, imunoestimulantes, antivirais e antitumorais. Não foram encontrados estudos avaliando a atividade diurética de U. tomentosa, e estudos pré-clínicos in vivo e ensaios clínicos serão necessários para avaliar esse possível potencial de U. tomentosa.

Keywords: *Uncaria tomentosa,* unha de gato, anti-inflamatórios e diuréticos.

ABSTRACT

The aim of this work was to review the literature regarding studies that evaluates the anti-inflammatory and diuretic activity of *Uncaria tomentosa* (Willd. DC.), popularly known as cat's claw. A search was made for scientific articles from September to August of 2017, using the descriptors: *Uncaria tomentosa*, cat's claw, diuretics and anti-inflammatories, as search strategies. In vivo preclinical studies and clinical trials were included in the evaluation of the anti-inflammatory and diuretic activity of *U. tomentosa*. From the 165 articles found, 10 are according to the inclusion criteria, 50% (n= 05) with experimental design in the form of pre-clinical in vivo tests, clinical trials corresponded to a total of 30% (n= 03) and the sample of In vivo and in vitro pre-clinical trials were equivalent to a total of 20% (n= 02). The most studied properties of *U. tomentosa* are anti-inflammatory, antioxidant, immune-stimulatory, antiviral and antitumor. No studies evaluating the diuretic activity of *U. tomentosa* were found, and pre-clinical in vivo studies and clinical trials will necessary to evaluate this possible *U. tomentosa* potential.

Keywords: *Uncaria tomentosa*, cat's claw, anti-inflammatories and diuretics.

[1] Especialista. Aluna do Programa de Mestrado em Ciências da Saúde, Universidade Federal do Tocantins.

E-mail: larissajcnutri@gmail.com

[2] Doutor. Laboratório de Ciências Básicas e da Saúde (LaCiBS), Universidade Federal do Tocantins.

1. INTRODUCTION

Uncaria tomentosa (Willd. DC.), popularly known as cat's claw, is a climbing shrub that can reach up to 35m in length and 5-40 cm in diameter at the base, grows supported on other trees using its semi-curved and pointed spikes in the shape of cat's claws (VALENTE, 2009). It belongs to the *Uncaria* genus and the *Rubiaceae* family, with a wide geographic distribution in the Amazon and Central America, including Bolivia, Brazil, Colombia, Costa Rica, Ecuador, Panama, Peru and Venezuela. In Brazil, it is present in the states of Acre, Amapá, Amazonas and Pará (MIRANDA et al., 2003, POLLITO, 2004, CARVALHO et al., 2015, DE PAULA et al., 2015).

U. tomentosa has been used for centuries in the form of bark, stem or root tea by indigenous tribes of the Amazon rainforest described, used for anti-inflammatory, immune-modulating and antioxidant purposes, used in the treatment of diseases such as osteoarthritis, cancer, viral infections, ulcers gastric and menstrual disorders. (REIS et al., 2008; SOUZA, CIMERMAN, 2010; DREIFUSS et al, 2013; CARVALHO et al., 2015)

Scientific studies attribute the therapeutic action of *U. tomentosa* to the presence of bioactive compounds, such as tetracyclic and pentacyclic oxindole alkaloids (POAs) with antioxidant, immunomodulatory and antineoplastic effects, associated with the power of UT to reduce oxidative stress and transcription factor expression (NF-κB), which regulates the expression of various pro-inflammatory cytokines including TNF-a, IL-1, IL-2, IL-6 and IL-8, enhancing their anti-inflammatory action (AKESSON, 2003; ALLEN-HALL, 2007, DE PAULA, el al., 2015).

The pharmacological activity of *U. tomentosa* can also be justified by the synergistic action of its compounds, such as polyphenols, phytosterols, glycosides and triterpenes of quinovic acid, which can inhibit viral infections, and procyanidins with antioxidant potential, anti-inflammatory properties antiviral drugs. (SANDOVAL, et al., 2000, DE PAULA, et al., 2015).

The present review aims to search the literature for studies that evaluate the anti-inflammatory and diuretic activity of *U. tomentosa*.

2. MATERIALS E METHODS

A search on the MEDLINE, LILACS and SCIELO databases was performed from August to September 2017, using the descriptors: *Uncaria tomentosa*, cat's claw, diuretics

and anti-inflammatories, with the following search strategy: *uncaria tomentosa and unha de gato, uncaria tomentosa and diuréticos, uncaria tomentosa and anti-inflamatórios, uncaria tomentosa and cat's claw, uncaria tomentosa and diuretic, uncaria tomentosa and anti-inflammatory, uncaria tomentosa and uñas de gato, uncaria tomentosa and diuréticos, uncaria tomentosa and anti-inflamatórios.*

The search terms were used in English, Portuguese and Spanish. Manual searches were made in the bibliographic references of the articles found. In order to include the articles, the following criteria were used: in vivo pre-clinical studies and clinical trials, whose outcome was the evaluation of *U. tomentosa's* anti-inflammatory and diuretic activity, investigated by in vivo experimental trials (human or animals), in which the objectives included the prevalence of the outcome and/or the associated factors, with a clearly described methodology, with population, carried out in scenarios of Brazilian or foreign territory, published in English, Portuguese or Spanish 1997 to 2017, with original articles available in full.

We excluded studies whose outcome was ethno-pharmacological, chemical and/or phytochemical identification, purification studies, abstracts of congresses and books.

After consulting the databases and the application of the search strategies, the studies that showed duplication between the bases and subsequent reading of the summaries of the resulting articles were identified and excluded. In cases where the summary reading was not sufficient to establish whether the article should be included, considering the defined inclusion criteria, the article was read in its entirety to determine its eligibility. When the summary was sufficient, the articles were selected and then obtained the full version for confirmation of eligibility and inclusion in the study.

For the extraction of the data of the articles, an instrument was elaborated containing the following information as: authors, year of publication, place of publication, language, type of study, population, sample size, characteristics and outcome.

3. RESULTS

After identification and selection of the 165 (n total) articles for systematic review and elimination of 30 duplicate articles, 135 articles were selected. From these, 91 were excluded after the analysis of titles and abstracts. From the 44 eligible articles, 34 were excluded for the following reasons: in 6 the characterization of bioactive compounds of *U. tomentosa* extracts was carried out; 2 concerning chemical composition; 3 evaluated

anticancer activity; 7 referred to the potential of immunomodulation; 2 were book chapters and 14 in vitro articles. At the end, 10 articles were included in the present systematic review, as described in figure 1.

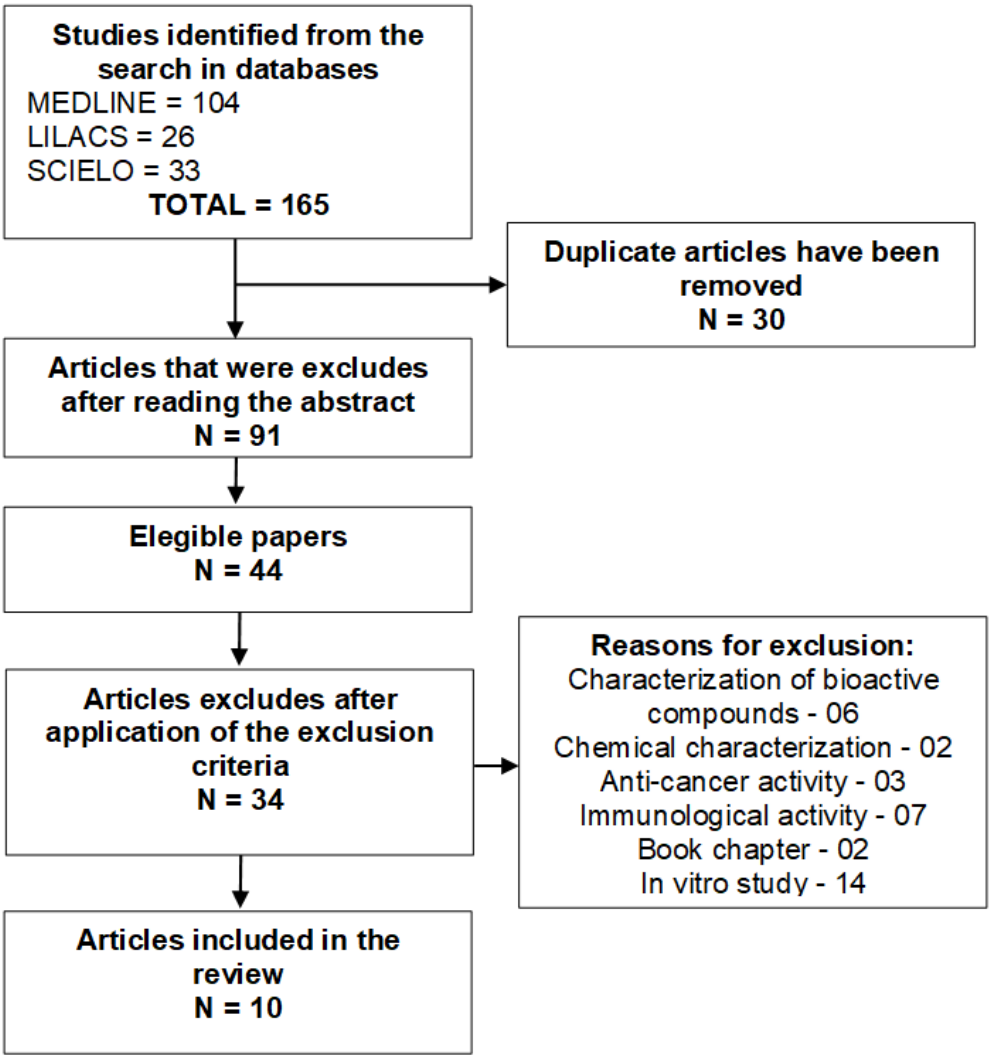

Figure 1. Identification and selection of articles for systematic review of the anti-inflammatory and diuretic activity of *U. tomentosa* (cat's claw).

After applying the exclusion criteria, a total of 10 articles were selected to carry out the review, figure 2 illustrates the design of the articles, 50% (n= 05) with experimental design in the form of pre-clinical trials in (n= 03), and the in-vivo and in-vitro preclinical sample size corresponded to a total of 20% (n= 02).

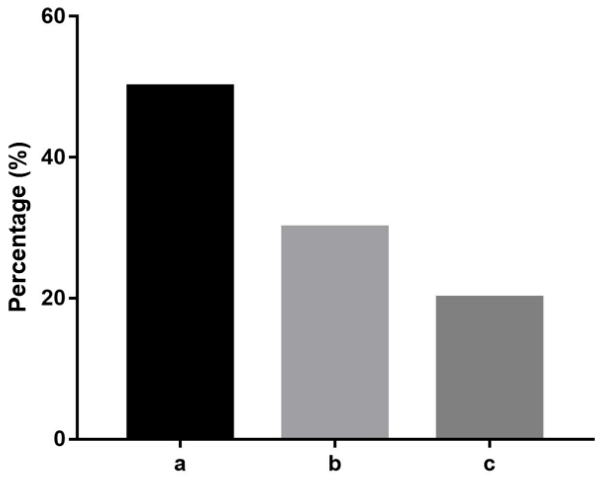

Figura 2. Design of included articles for systematic review of the anti-inflammatory and diuretic activity of U. *tomentosa* (cat's claw).

Legend: (a - pre-clinical trials, in vivo, b - clinical trials, c- pre-clinical trials, in vivo and in vitro)

The studies found refer to the anti-inflammatory potential of *U. tomentosa*, review articles, in vivo pre-clinical studies, and clinical trials evaluating its diuretic activity were not found.

Table 1 presents the synthesis of the characteristics of the studies included in the systematic review. As for the general characteristics, the oldest publication was from 2001 and the most recent one referring to the year 2016. The predominant language was English with 90% (n= 09) of the publications and 10% (n= 01) published in Portuguese. Brazil corresponded to the country with the highest percentage among publications 50% (n= 05).

The interventions used in the form of *U. tomentosa* extract or decoction, in varied doses, according to the experimental protocol of each study, characteristics regarding the objective of the research and conclusion, indicating in 100% of the articles, a probable anti- inflammatory.

Table 1. Characteristics of selected studies on the anti-inflammatory and diuretic activity of *uncaria tomentosa* (cat's claw) according to author, year, place, language, study design, sample duration, dosage, expected outcome and completion, Brazil, 1997 to 2017.

Author/year Place/Language	**Type of study and population**	**Duration**	**Features**	**Conclusion**
PISCOYA et al., 2001. The United States / English.	Clinical trial 45 individuals, male (45-75 years).	4 weeks.	To evaluate the ability of *U. tomentosa* in the treatment of knee osteoarthritis, safety and tolerance and comparison of the anti-inflammatory and anti-inflammatory action of *U. guianensis* and *U. Tomentosa*	Effective treatment for osteoarthritis, are effective antioxidants, and their anti-inflammatory properties may result from the ability to inhibit TNF-a ± and, to a lesser extent, PGE2 production.
AGUILAR et al., 2002. Peru/ English.	In vivo and in vitro pre-clinical assay 96 rats, female.	8 days.	Evaluation of the anti-inflammatory activity of two different extracts of *U. tomentosa*.	Anti-inflammatory activity in both extracts, this activity being much more evident with the hydroalcoholic extract.
MUR et al., 2002., Austria/ English.	Clinical trial. 40 patients, 87% female. 21 received an extract and 19 received a placebo.	52 weeks.	Evaluation of the safety and efficacy of a U. tomentosa extract in patients with active rheumatoid arthritis (RA)	*U. tomentosa* extract showed no toxicity and reduced number of painful joints when it is compared to placebo in RA patients.
AKESSON; PERO; IVARS, 2003. Sweden/ English.	In vivo and in vitro pre-clinical assay 6 female rats.	6-8 weeks.	Impact assessment of C-Med 100® in the immune system, induced mechanisms involved in accelerating recovery of leucopenia.	Potential agent to clinically accelerate the recovery of patients with leukopenia. Anti-inflammatory effects may be due to inhibition of TNFa production.
CISNEROS; JAYO; NIEDZIELA, 2005. The United States/ english.	In vivo pre-clinical trial 136 rats, male.	8 days.	Anti-inflammatory potential of U. Tomentosa in prevention or modulation Pulmonary injury induced by Ozone.	It conferred protection to the bronchiolar epithelium of the lung and could be indicative of anti-inflammatory activity or modulation of O3-induced lung injury.
MFF et al., 2011. Brazil/ portuguese.	In vivo Pre-clinical test, 35 rats, male.	5 days.	Evaluation of the renoprotective effect of *U. tomentosa* on renal function, urinary excretion of peroxides and malondelated rat with experimentally induced ischemic LRA.	Treatment with *U. tomentosa* promoted functional protection assessed by increased clearance of creatinine, reduction of urinary peroxidation and TBARS, which may be related to the antioxidant and anti-inflammatory activities of the herbal remedy.

(continuation)

Author/year Place/Language	**Type of study and population**	**Duration**	**Features**	**Conclusion**
ROJAS-DURAN et al., 2012. France/ english.	Preclinical in vivo test, 18 female rats.	3 days.	To evaluate the anti-inflammatory activity of mitrafilaína, an alkaloid isolated from U. Tomentosa.	Inhibition of nuclear factor-kB activation (NF-kB), which regulates immune and anti-inflammatory responses. It can be a new component for the development of anti-inflammatory treatment.
DREIFUSS et al., 2013. Brazil/ english .	Preclinical test, 18 male mice.	14 days.	To compare the anti-neoplastic effects of a crude hydrocolloidal extract (BBB) *Uncaria tomentosa* (UT) with the two fractions derived, tested against the primary tumor of the Walker-256 strain Dreifussmodulation of oxidative stress.	Expressive anti-neoplastic and antioxidant activity and indicate an anti-inflammatory activity. In total, the reduction of TNF-a cytokine some characteristics of this tumor.
DE PAULA et al., 2015. Brazil/ english.	Phase II clinical trial. 51 individuals (33 to 85 years-old), 47% female.	8 weeks.	Evaluation of the anti-inflammatory and antitumor activity of U. tomentosa in the treatment of symptoms of patients with terminal cancer	The use of *U. tomentosa* may be beneficial in patients with advanced cancer, improving its quality of life and reduced fatigue. The mechanism of action does not appear to be related to the anti-inflammatory property of the plant.
DIETRICH et al., 2015. Brazil/ english.	In vivo Pre-clinical trial. 446 rats, male.	6 weeks.	To investigate the potential therapeutic effect of the purified fraction of quinovic acid glycosides in rats with induced hemorrhagic cystitis (CH).	It had a protective effect on urothelial damage induced by control of visceral pain, reduction of IL-1β levels and regulation of P2X7 receptors. Promising anti-inflammatory properties.

4. DISCUSSION

In vivo pre-clinical trials and Phase II clinical studies performed on humans have demonstrated safety, characterizing *U. tomentosa* of a non-toxic nature and the pharmacological control, anti-inflammatory properties are well known through their beneficial effects on the treatment of chronic inflammatory diseases such as osteoarthritis and rheumatoid arthritis (PISCOYA et al., 2001, MUR, E et al., 2002, DE PAULA et al., 2015).

U. tomentosa extract was used in a clinical study with 45 individuals with osteoarthritis of the knee, in order to evaluate its anti-inflammatory and antioxidant effects, demonstrating an effective treatment with rapid reduction of pain and improved function, attributing that its anti-inflammatory properties inflammatory agents may result from the ability to inhibit TNFÎ ± and, to a lesser extent, the production of PGE2 (PISCOYA et al., 2001).

The main component of the *U. tomentosa* that confers immune-stimulatory potential are the oxindolic and indole alkaloids, and the quinovocal glycosides are the ones that present anti-inflammatory and antioxidant activity, pointed out in a study evaluating the renoprotective effect in induced ischemic injury in rats, as a cellular repair factor, acting through the high concentration of flavonoids that sequester reactive oxygen species, reducing oxidative stress and inflammation, conferring protective effect (MFF et al., 2011).

In a pre-clinical study in vivo, AGUILAR et al. (2002) compared the hydro-alcoholic extract and lyophilized aqueous extract at different concentrations for 8 days. Using 96 rats, extracts were shown to inhibit the activation of nuclear factor-kB (NF-kB), which regulates host immune and anti-inflammatory responses.

Rats with ozone-induced inhalation pneumonitis were treated with *U. tomentosa* by observing a significant reduction in epithelial necrosis content and mainly neutrophil polymorphonuclear macrophages, present in acute inflammation, conferring protection to the bronchiolar epithelium of the lung, and may be indicative of activity anti-inflammatory or modulation of O3-induced lung injury. (CISNEROS, 2005).

Quinobic acid glycosides have been shown to reduce edema, hemorrhage, IL-1B rates and neutrophil migration during hemorrhagic cystitis (HC) in rats, showing protective effect on CH-induced urothelial damage, control of visceral pain, reduction of IL-1β levels and regulation of P2X7 receptors, characterizing promising anti-inflammatory properties of

U. tomentosa, contributing to the treatment of respiratory and urinary tract infections, which are common clinical conditions (DIETRICH, 2015).

A double-phase, randomized, double-blind clinical trial demonstrated that the use of a *U. tomentosa* extract, which is rich in pentacyclic oxindole alkaloids, showed a significant reduction in the number of painful and swollen joints compared to placebo between patients with rheumatoid arthritis (53.2% vs. 24.1%) (MUR et al., 2002).

The evaluation of the anti-inflammatory and antitumor activity of *U. tomentosa* in the treatment of symptoms of patients with terminal cancer pointed improvement in quality of life, reduced fatigue and body weight of patients stabilized as a result after intervention through the ingestion of *U. tomentosa* extract. The mechanism of action seems to be related to its anti-inflammatory properties (DE PAULA et al., 2015).

The relation of the evidenced properties to *U. tomentosa*, among them, the anti-inflammatory action, ratifies and fosters a greater security of the popular use.

5. FINAL CONSIDERATIONS

The most studied properties of *U. tomentosa* are anti-inflammatory, antioxidant, immune-stimulatory, antiviral and antitumor. No studies were found to evaluate its diuretic activity, but its anti-inflammatory potential, recorded in the literature, allows a better understanding of the extent of its effects and the consequent improvement of the requirements for the treatment of inflammatory conditions.

REFERENCES

AGUILAR, J. L. et al. **Anti-inflammatory activity of two different extracts of Uncaria tomentosa (Rubiaceae)**. Journal of Ethnopharmacology, v. 81, n. 2, p. 271–276, 2002.

AKESSON, C; LINDGREN, H; PERO, R.W, et al. **An extract of Uncaria tomentosa inhibiting cell Division and NF-kappa B activity without inducing cell death**. Int Immunopharmacol,3:1889–1900, 2003.

AKESSON, C.; PERO, R. W.; IVARS, F. **C-Med 100, a hot water extract of Uncaria tomentosa, prolongs lymphocyte survival in vivo**. Phytomedicine : international journal of phytotherapy and phytopharmacology, v. 10, n. 1, p. 23–33, 2003.

ALLEN-HALL, L; CANO, P; ARNASON, J.T; et al. **Treatment of THP-1 cells with Uncaria tomentosa extracts differentially regulates the expression if IL-1beta and TNF-alpha**. J Ethnopharmacol, 109:312–317, 2007.

CARVALHO, L.C.L.P; FONSECA, F; PERAZZO, F et al. **Uncaria Tomentosa (Cat's Claw) improves quality of life in patients with Advanced solid tumors**. The Journal of Alternative and Complementary Medicine*, 21:22-30, 2015.*

CISNEROS, F. J.; JAYO, M.; NIEDZIELA, L. **An Uncaria tomentosa (cat's claw) extract protects mice against ozone-induced lung inflammation**. Journal of Ethnopharmacology, v. 96, n. 3, p. 355–364, 2005.

DE PAULA, L. C. L. et al. ***Uncaria tomentosa* (Cat's Claw) Improves Quality of Life in Patients with Advanced Solid Tumors**. The Journal of Alternative and Complementary Medicine, v. 21, n. 1, p. 22–30, 2015.

DIETRICH, F. et al. **The quinovic acid glycosides purified fraction from uncaria tomentosa protects against hemorrhagic cystitis induced by cyclophosphamide in mice**. PLoS ONE, v. 10, n. 7, p. 1–15, 2015.

DREIFUSS, A. A. et al. **Uncaria tomentosa Exerts Extensive Anti-Neoplastic Effects against the Walker-256 Tumour by Modulating Oxidative Stress and Not by Alkaloid Activity**. PLoS ONE, v. 8, n. 2, 2013.

EROWELE, G.I; KALEJAIYE, A.O. **Pharmacology and therapeutic uses of cat's claw**. Am J Health Syst Pharm, Jun 1;6(1):992-5, 2009.

MFF, V. et al. **Uncária tomentosa e a lesão renal aguda isquêmica em ratos Uncária tomentosa e a lesão renal aguda isquêmica em ratos**. Rev Esc Enferm USP, v. 45, n. 1, p. 194–8, 2011.

MIRANDA, E.M.; SOUSA, J.A.; PEREIRA, R.C.A. **Caracterização e avaliação de populações nativas de unhade-gato [Uncaria tomentosa (Willd.) DC. e U. guianensis (Aubl.) Gmel.] no vale do rio Juruá-AC**. Revista Brasileira de Plantas Medicinais, v.5, p.41-46, 2003.

MUR, E. et al. **Randomized double-blind trial of an extract from the pentacyclic alkaloid-chemotype of Uncaria tomentosa for the treatment of rheumatoid arthritis**. J Rheumatol 29(4):678–681, 2002.

PISCOYA, J. et al. **Efficacy and safety of freeze-dried cat's claw in osteoarthritis of the knee: Mechanisms of action of the species Uncaria guianensis**. Inflammation Research, v. 50, n. 9, p. 442–448, 2001.

POLLITO, P.A.Z. **Dendrologia, anatomia do lenho e status de conservação das espécies lenhosas dos gêneros Cinchona, Croton e Uncaria no estado do Acre,**

Brasil. 181p. Tese Doutorado, Escola Superior de Agricultura Luiz de Queiroz, Universidade de São Paulo, 2004.

REIS, S.R; VALENTE, L.M; SAMPAIO, A.L, SIANI, A.C; GANDINI, M; AZEREDO, E.L et al. **Immunomodulating and antiviral activities of Uncaria tomentosa on human monocytes infected with Dengue Virus-2**. Int Immunopharmacol, 8(3):468-76, 2008.

ROJAS-DURAN, R. et al. **Anti-inflammatory activity of Mitraphylline isolated from Uncaria tomentosa bark**. Journal of Ethnopharmacology, v. 143, n. 3, p. 801–804, 2012.

SANDOVAL, M; CHARBONNET, R.M; OKUHAMA, N.N, el al. **Cat's claw inhibits TNF alpha production and scavenges free radicals: role in cytoprotection**. Free Radic Biol Med, 29:71–78, 2000.

SOUZA, A.L. de; CIMERMAN, S. **Uncaria tomentosa (Cat's claw): um potencial estratégia terapêutica para herpes labial**. Revista Panamericana de Infectologia. v.12, n.2, p.51-57, 2010.

VALENTE, L. M. M. **Unha-de-gato [*Uncaria tomentosa* (Willd.) DC. e *Uncaria guianensis* Aubl.) Gmel.]: Um panorama sobre seus aspectos mais relevantes**. Revista Fitos Eletrônica, [S.l.], v. 2, n. 01, p. 48-58, jun/set. 2006. ISSN 2446-4775. Disponível em: http://revistafitos.far.fiocruz.br/index.php/revista-fitos/article/view/40/pdf_32. Acesso em: 15 jul. 2017.

VATTIMO, M. F. F; SILVA, N. O. **Uncária tomentosa e a lesão renal aguda isquêmica em rato**. Revista da Escola de Enfermage da USP, v.45, n.1,p.194 -8, 2011.