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## List of references supporting the assessment of *Uncaria tomentosa* (Willd. Ex Schult.) DC., cortex

Draft

**The European Medicines Agency acknowledges that copies of the underlying works used to produce this monograph were provided for research only with exclusion of any commercial purpose.**

Abe S, Ishibashi H, Masuo K, Tanaka S, Yamaguchi H. [Suppression of carrageenan-induced edema by oral administration of extracts of *Uncaria tomentosa* and/or *Harpagophytum procumbens*.] *Pharmacometrics* 2002, 62(2/3):27-31 [Japanese]

Aguilar JL, Rojas P, Marcelo A, Plaza A, Bauer R, Reiningger E *et al.* Anti-inflammatory activity of two different extracts of *Uncaria tomentosa* (Rubiaceae). *Journal of Ethnopharmacology* 2002, 81(2):271-276

Åkesson C, Lindgren H, Pero RW, Leanderson T, Ivars F. An extract of *Uncaria tomentosa* inhibiting cell division and NF-kappa B activity without inducing cell death. *International Journal of Immunopharmacology* 2003a, 3(13-14):1889-1900

Åkesson C, Lindgren H, Pero RW, Leanderson T, Ivars F. Quinic acid is a biologically active component of the *Uncaria tomentosa* extract C-Med 100. *International Journal of Immunopharmacology* 2005, 5(1):219-229

Åkesson C, Pero RW, Ivars F. C-Med 100, a hot water extract of *Uncaria tomentosa*, prolongs lymphocyte survival *in vivo*. *Phytomedicine* 2003b, 10(1):23-33

Allen-Hall L, Arnason JT, Cano P, Lafrenie RM. *Uncaria tomentosa* acts as a potent TNF-alpha inhibitor through NF-kappaB. *Journal of Ethnopharmacology* 2010, 127(3):685-693

Allen-Hall L, Cano P, Arnason JT, Rojas R, Lock O, Lafrenie RM. Treatment of THP-1 cells with *Uncaria tomentosa* extracts differentially regulates the expression of IL-1beta and TNF-alpha. *Journal of Ethnopharmacology* 2007, 109(2):312-317

Aquino R, De Simone F, Pizza C, Conti C, Stein ML. Plant metabolites. Structure and *in vitro* antiviral activity of quinic acid glycosides from *Uncaria tomentosa* and *Guettarda platypoda*. *Journal of Natural Products* 1989, 52(4):679-685



- Aquino R, De Feo V, De Simone F, Pizza C, Cirino G. Plant metabolites. New compounds and anti-inflammatory activity of *Uncaria tomentosa*. *Journal of Natural Products* 1991, 54(2):453-459
- Aquino R, De Tommasi N, De Simone F, Pizza C. Triterpenes and quinovic acid glycosides from *Uncaria tomentosa*. *Phytochemistry* 1997, 45(5):1035-1040
- Araújo MdoCS, Farias IL, Gutierrez J, Dalmora SL, Flores N, Farias J *et al.* *Uncaria tomentosa*-Adjuvant Treatment for Breast Cancer: Clinical Trial. *Evidence-based Complementary and Alternative Medicine* 2012, Article ID:676984, 8 pages, doi:10.1155/2012/676984
- Badilla B, Chaves F, Mora G, Poveda LJ. Edema induced by *Bothrops asper* (Squamata: Viperidae) snake venom and its inhibition by Costa Rican plant extracts. *Revista de Biología Tropical* 2006, 54(2):245-252
- Barnes J, Anderson LA, Phillipson JD. Herbal Medicines. 2<sup>nd</sup> ed. Pharmaceutical Press, London, Chicago 2002
- Bednarek D, ŁLukasiak J, Kondracki M, Zurowska K, Falkiewicz B, Niemczuk K: Modulating effects of *Uncaria tomentosa* in experimentally-induced local pneumonia in calves. *Bulletin of the Veterinary Institute of Pulawy* 2002, 46:65-77
- Belteghi C.G., Manzat R.M.. Study regarding the immunoadjuvant qualities of an *Uncaria tomentosa*-based product. *Lucrări Stiințifice Medicină Veterinară* VOL. XLI, 2008, 41:255-263 TIMISOARA
- Bigliani MC, Rosso MC, Zunino PM, Baiardi G, Ponce AA. Anxiogenic-like effects of *Uncaria tomentosa* (Willd.) DC. aqueous extract in an elevated plus maze test in mice: a preliminary study. *Natural Product Research* 2013, 27(18):1682-1685
- Bižanov G, Tamošiūnas V. Immune Responses Induced in Mice after Intragastral Administration with Sendai Virus in Combination with Extract of *Uncaria tomentosa*. *Scandinavian Journal of Laboratory Animal Science* 2005, 32(4):201-207
- Blaschek W, Hänsel R, Keller K, Reichling J, Rimpler H, Schneider G, editors. Hagers Handbuch der Pharmazeutischen Praxis. Drogen L-Z. Vol. 3. 5<sup>th</sup> ed. Springer-Verlag, Berlin 1998
- Bors M, Bukowska B, Pilarski R, Gulewicz K, Oszmianski J, Michałowicz J, Koter-Michalak M. Protective activity of the *Uncaria tomentosa* extracts on human erythrocytes in oxidative stress induced by 2,4-dichlorophenol (2,4-DCP) and catechol. *Food and Chemical Toxicology* 2011, 49(9):2202-2211
- Bors M, Michałowicz J, Pilarski R, Sicinska P, Gulewicz K, Bukowska B. Studies of biological properties of *Uncaria tomentosa* extracts on human blood mononuclear cells. *Journal of Ethnopharmacology* 2012a, 142(3):669-678
- Bors M, Sicinska P, Michałowicz J, Wieteska P, Gulewicz K, Bukowska B. Evaluation of the effect of *Uncaria tomentosa* extracts on the size and shape of human erythrocytes (*in vitro*). *Environmental Toxicology and Pharmacology* 2012b, 33(2):127-134
- Budán F, Szabó I, Varjas T, Nowrasteh G, Dávid T, Gergely P, Varga Z, Molnár K, Kádár B, Orsós Z, Kiss I, Ember I.: Mixtures of *Uncaria* and *Tabebuia* extracts are potentially chemopreventive in CBA/Ca mice: a long-term experiment. *Phytotherapy Research* 2011 25(4):493-500
- Budzinski JW, Foster BC, Trudeau VL, Drouin CE, Bafi-Yebo N, Arnason JT. The Interaction of Selected Phytochemicals, HIV Drugs, and Commercial-Source Herbal Teas and Capsules with Human Cytochrome P450 3A4 and P-glycoprotein. *Pharmaceutical Biology* 2008, 46(1-2):53-65

Budzinski JW, Foster BC, Vandenhoeck S, Arnason JT. An *in vitro* evaluation of human cytochrome P450 3A4 inhibition by selected commercial herbal extracts and tinctures. *Phytomedicine* 2000, 7(4):273–282

Bukowska B, Bors M, Gulewicz K, Koter-Michalak M. *Uncaria tomentosa* extracts protect human erythrocyte catalase against damage induced by 2,4-D-Na and its metabolites. *Food and Chemical Toxicology* 2012, 50(6):2123-2127

Cabieses F. The Saga of the Cat's Claw. Via Lactera Editores, Lima 1994

Caldas LQA, Olej B, Slomp H, Timóteo MO, Velarde LG, Duarte H *et al.* *Uncaria tomentosa* in the Treatment of the Herpes Labialis: Randomized Double-Blind Trial. *DST - Journal Brasileiro de Doenças Sexualmente Transmissíveis* 2010, 22(2):57-59

Caon T, Kaiser S, Feltrin C, de Carvalho A, Sincero TC, Ortega GG, Simoes CM. Antimutagenic and antiherpetic activities of different preparations from *Uncaria tomentosa* (cat's claw). *Food and Chemical Toxicology* 2014, 66:30-35

Castañeda DO, León G, León D, Calvo A, Chávez J, Escalante J *et al.* Uña de Gato en Artritis Reumatoide: Estudio doble ciego, en comparación con placebo. *Revista Peruana de Reumatología* 1998, 4(1):15-21 [Spanish]

Castillo GM, Choi PY, Cummings JA, Snow AD. Inhibition of Parkinson's disease alpha synuclein fibrillogenesis by PTI-777. *Society for New Neuroscience Abstracts* 2001, 27:608

Chen CX, Jin RM, Li YK, Zhong J, Yue L, Chen SC, *et al.* Inhibitory effect of rhynchophylline on platelet aggregation and thrombosis. *Acta Pharmacologica Sinica* 1992, 13(2):126-130

Cheng AC, Jian CB, Huang YT, Lai CS, Hsu PC, Pan MH. Induction of apoptosis by *Uncaria tomentosa* through reactive oxygen species production, cytochrome c release, and caspases activation in human leukemia cells. *Food and Chemical Toxicology* 2007, 45(11):2206-2218

Cisneros FJ, Jayo M, Niedziela L. An *Uncaria tomentosa* (cat's claw) extract protects mice against ozone-induced lung inflammation. *Journal of Ethnopharmacology* 2005, 96(3):355-364

Cosentino C, Torres L. Reversible worsening of Parkinson disease motor symptoms after oral intake of *Uncaria tomentosa* (cat's claw). *Clinical Neuropharmacology* 2008, 31(5):293-294

Cummings JA, Castillo GM, Choi PY, Snow AD. Disruption of pre-deposited Alzheimer's  $\text{A}\beta$  1–42 fibrils by PTI-00703 (cat's claw derivative) in a rodent model of  $\text{A}\beta$  fibrillogenesis. *Neurobiology of Aging* Suppl. 1. 2000, 21:153

Cupp MJ, editor. Toxicology and Clinical Pharmacology of Herbal Products. Humana, Totowa, NY 2000

Deharo E, Baelmans R, Gimenez A, Quenevo C, Bourdy G. *In vitro* immunomodulatory activity of plants used by the Tacana ethnic group in Bolivia. *Phytomedicine* 2004, 11(6):516-522

De Martino L, Martinot JL, Franceschelli S, Leone A, Pizza C, De Feo V. Proapoptotic effect of *Uncaria tomentosa* extracts. *Journal of Ethnopharmacology* 2006, 107(1):91-94

Domingues A, Sartori A, Golimc MA, Valente LMM, da Rosa LC, Ishikawa LLV, *et al.* Prevention of experimental diabetes by *Uncaria tomentosa* extract: Th2 polarization, regulatory T cell preservation or both? *Journal of Ethnopharmacology* 2011a, 137(1):635-642

- Domingues A, Sartori A, Valente LM, Golim MA, Siani AC, Viero RM. *Uncaria tomentosa* aqueous-ethanol extract triggers an immunomodulation toward a Th2 cytokine profile. *Phytotherapy Research* 2011b, 25(8):1229-1235
- Dreifuss AA, Bastos-Pereira AL, Ávilab TV, Soley Bda S, Riveroc AJ, Aguilara JL *et al.* Antitumoral and antioxidant effects of a hydroalcoholic extract of cat's claw (*Uncaria tomentosa*) (Willd. Ex Roem. & Schult) in an *in vivo* carcinosarcoma model. *Journal of Ethnopharmacology* 2010, 130(1):127–133
- Dreifuss AA, Bastos-Pereira AL, Fabossi IA, Livero FA, Stolf AM, Alves de Souza CE *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* 2013, 8(2):e54618
- Eberlin S, dos Santos LM, Queiroz ML. *Uncaria tomentosa* extract increases the number of myeloid progenitor cells in the bone marrow of mice infected with *Listeria monocytogenes*. *International Journal of Immunopharmacology* 2005, 5(7-8):1235-1246
- Erowele GI, Kalejaiye AO. Pharmacology and therapeutic uses of cat's claw. *American Journal Health-System Pharmacy* 2009, 66(11):992-995
- Farias IL, Araújo MdoCS, Farias JG., Rossato LV, Elsenbach LI, Dalmora SL, *et al.* *Uncaria tomentosa* for Reducing Side Effects Caused by Chemotherapy in CRC Patients: Clinical Trial. *Evidence-Based Complementary and Alternative Medicine* 2012, Article ID 892182, 8 pages, doi:10.1155/2012/89218
- Farias I, Araujo MdoCS, Zimmermann ES, Dalmora SL, Benedetti AL, Alvarez-Silva M, *et al.* *Uncaria tomentosa* stimulates the proliferation of myeloid progenitor cells. *Journal of Ethnopharmacology* 2011, 137(1):856-863
- Foster BC, Vandenhoeck S, Hana J, Krantis AAKhtar MH, Bryan M *et al.* *In vitro* inhibition of human cytochrome P450-mediated metabolism of marker substrates by natural products. *Phytomedicine* 2003, 10(4):334-342
- Fraçkowiak T, Baczek T, Roman K, Zbikowska B, Glensk M, Fecka I, *et al.* Binding of an oxindole alkaloid from *Uncaria tomentosa* to amyloid protein (Aβ<sub>1-40</sub>). *Zeitschrift für Naturforschung C* 2006, 61(11-12):821-826
- Gan R, Dong G, Yu J, Wang X, Fu S, Yang S. Protective Effects of Isorhynchophylline on Cardiac Arrhythmias in rats and guinea pigs. *Planta Medica* 2011, 77(13):1477-1481
- García R, Cayunao C, Bocic R, Backhouse N, Delporte C, Zaldivar M, *et al.* Antimicrobial activity of isopteropodine. *Zeitschrift für Naturforschung C* 2005, 60(5-6):385-388
- Gertz MA, Bauer B. A The art of oncology: when the tumor is not the target Caring (Really) for Patients Who Use Alternative Therapies for Cancer. *Journal of Clinical Oncology* 2001, 19(23):4346-4349
- Gimenez D, Garcia Prado E, Saenz Rodriguez T, Fernandez Arche A, De la Puerta R. Cytotoxic effect of the pentacyclic oxindole alkaloid mitraphylline isolated from *Uncaria tomentosa* bark on human Ewing's sarcoma and breast cancer cell lines. *Planta Medica* 2010, 76(2):133-136
- Gonçalves C, Dinis T, Batista MT. Antioxidant properties of proanthocyanidins of *Uncaria tomentosa* bark decoction: a mechanism for anti-inflammatory activity. *Phytochemistry* 2005, 66(1):89–98
- Gonzales GF, Valerio LG Jr. Medicinal Plants from Peru: A Review of Plants as Potential Agents Against Cancer. *Anti-Cancer Agents in Medicinal Chemistry* 2006, 6(5):429-444

Gardner Z, McGuffin M, editors. American Herbal Products Association's botanical safety handbook. 2<sup>nd</sup> ed. CRC press, Boca Raton 2013

Groom SN, Johns T, Oldfield PR. The potency of immunomodulatory herbs may be primarily dependent upon macrophage activation. *Journal of Medicinal Food* 2007, 10(1):73-79

Gurrola-Diaz CM, Garcia-Lopez PM, Gulewicz K, Pilarski R, Dihlmann S. Inhibitory mechanisms of two *Uncaria tomentosa* extracts affecting the Wnt-signaling pathway. *Phytomedicine* 2011, 18(8-9):683-690

Guthrie OW, Gearhart CA, Fulton S, Fechter LD. Carboxy alkyl esters of *Uncaria tomentosa* augment recovery of sensorineural functions following noise injury. *Brain Research* 2011, 1407:97-106

Heitzman ME, Neto CC, Winiarz E, Vaisberg AJ, Hammond GB. Ethnobotany, phytochemistry and pharmacology of *Uncaria* (Rubiaceae). *Phytochemistry* 2005, 55:5-29

Hilepo JN, Bellucci AG, Mossey RT. Acute renal failure caused by 'cat's claw' herbal remedy in a patient with systemic lupus erythematosus. *Nephron* 1997, 77(3):61

Holderness J, Jackiw L, Kimmel E, Kerns H, Radke M, Hedges JF, *et al.* Select plant tannins induce IL-2/Ralpha up-regulation and augment cell division in gamma/delta T cells. *Journal of Immunology* 2007, 179(10):6468-6478

Ibrahim KE, Al-Ashban RM, El-Sammani SA. A Study of the Toxicity of Cat's Claw Herbal Medicine. *Research Journal of Pharmacology* 2009, 3(3):52-57

Jin RM, Chen CX, Li YK, Xu PK.. [Effect of rhynchophylline on platelet aggregation and experimental thrombosis.] *Yao Xue Xue Bao* 1991, 26(4):246-249 [Chinese]

Jürgensen S, Dalbo S, Angers P, Santos AR, Ribeiro-do-Valle RM. Involvement of 5-HT<sub>2</sub> receptors in the antinociceptive effect of *Uncaria tomentosa*. *Pharmacology, Biochemistry and Behavior* 2005, 81(3):466-477

Kang TH, Murakami Y, Matsumoto K, Takayama H, Kitajima M, Aimi N, *et al* Rhynchophylline and isorhynchophylline inhibit NMDA receptors expressed in *Xenopus* oocytes. *European Journal of Pharmacology* 2002a, 455(1):27-34

Kang TH, Matsumoto K, Tohda M, Murakami Y, Takayama H, Kitajima M, *et al.* Pteropodine and isopteropodine positively modulate the function of rat muscarinic M(1) and 5-HT(2) receptors expressed in *Xenopus* oocyte. *European Journal of Pharmacology* 2002b, 444(1-2):39-45

Kantani H, Kohda H, Yamasaki K, Hotta I, Nakata Y, Segawa T *et al.* The principles of the branchlet and hook of *Uncaria sinensis* Oliv. examined with a 5-hydroxytryptamine receptor binding assay. *The Journal of Pharmacy in Pharmacology* 1985, 37(6):401-404

Kemper K. J. Cat's Claw (*Uncaria tomentosa*). *Longwood Herbal Task Force* 1999, 1-13

Keplinger K, Laus G, Wurm M, Dierich MP, Teppner H. *Uncaria tomentosa* (Willd.) DC.—Ethnomedicinal use and new pharmacological, toxicological and botanical results. *Journal of Ethnopharmacology* 1999, 64(1):23–34

Keplinger K, Wagner H, Kreutzkamp B. Oxindole alkaloids having properties stimulating the immunological system and preparation containing the same. US Patent 4,940,725, 1990

- Kitajima M, Hashimoto K, Yokoya M, Takayama H, Sandoval M, Aimi N. Two new nor-triterpene glycosides from peruvian "Uña de Gato" (*Uncaria tomentosa*). *Journal of Natural Products* 2003, 66(2): 320-3
- Klinar SB, Castillo PR, Chang AC, Schmeda-Hirschmann G, Reyes S, Theoduloz C *et al.* Biological activity of medicinal plants of Ica (Perú). *Fitoterapia* 1995, 66(4):341-345
- Kloucek P, Polesny Z, Svobodova B, Vlkova E, Kokoska L. Antibacterial screening of some Peruvian medicinal plants used in Calleria District. *Journal of Ethnopharmacology* 2005, 99(2):309-312
- Kuras M, Nowakowska J, Sliwinska E, Pilarski R, Ilasz R, Tykarska T, *et al.* Changes in chromosome structure, mitotic activity and nuclear DNA content from cells of *Allium Test* induced by bark water extract of *Uncaria tomentosa* (Willd.) DC. *Journal of Ethnopharmacology* 2006, 107(2):211-221
- Lamm S, Sheng Y, Pero RW. Persistent response to pneumococcal vaccine in individuals supplemented with a novel water soluble extract of *Uncaria tomentosa*, C-Med-100<sup>®</sup>. *Phytomedicine* 2001, 8(4):267–274
- Laus G, Keplinger K. Separation of stereoisomeric oxindole alkaloids from *Uncaria tomentosa* by high performance chromatography. *Journal of Chromatography* 1994, 662:243 249
- Laus G, Keplinger K. Radix *Uncariae tomentosae* (Willd.) DC. *Zeitschrift für Phytotherapie* 1997, 18:122-126
- Lee KK, Zhou BN, Kingston DGI, Vaisberg AJ, Hammond GB. Bioactive Indole Alkaloids from the Bark of *Uncaria guianensis*. *Planta Medica* 1999, 65(8):759-760
- Lemaire I, Assinewe V, Cano P, Awang DV, Arnason JT. Stimulation of interleukin-1 and -6 production in alveolar macrophages by the neotropical liana, *Uncaria tomentosa* (una de gato). *Journal of Ethnopharmacology* 1999, 64(2):109-115
- Leon FR, Ortiz N, Atunéz de Mayalo A, Namisato T, Monge R. Antimutagenic activity of the freeze-dried aqueous extract of *Uncaria tomentosa* both in smokers and non-smokers. *Abstracts from the 3rd European Colloquium on Ethnopharmacology [and] 1st International Conference on Anthropology and History of Health and Disease Genova, Italy* 1996 Erga edizioni, p.255, poster
- Lopez Galera RM, Ribera Pascuet E, Esteban Mur JI, Montoro Ronsano JB, Juárez Giménez CJ. Interaction between cat's claw and protease inhibitors atazanavir, ritonavir and saquinavir. *European Journal of Clinical Pharmacology* 2008, 64(12):1235–1236
- Mammone T, Akesson C, Gan D, Giampapa V, Pero RW. A water soluble extract from *Uncaria tomentosa* (Cat's Claw) is a potent enhancer of DNA repair in primary organ cultures of human skin. *Phytotherapy Research* 2006, 20(3): 178-183
- McKenna DJ, Jones K, Hughes K, Humphrey S, editors. *Botanical Medicines. The desk reference for Major Herbal Supplements.* 2<sup>nd</sup> ed. The Haworth Herbal Press, Binghampton, NY, USA 2002
- Miller MJS, Zhang XJ, Charbonnet RM, Clark DA, Sandoval M. The anti-inflammatory actions of the herbal medicine, cat's claw, are due to a suppression of NF-κB activation and inhibition of gene expression. *Paediatric Research* 1999, 45:114A (*Gastroenterology and nutrition platform*, abstract 659)
- Mimaki Y, Toshimizu N, Yamada K, Sashida Y. [Anti-convulsion effects of choto-san and choko (*Uncariae Uncis cam Ramlus*) in mice, and identification of the active principles.] *Yakugaku Zasshi* 1997, 117(12):1011-1021 [Japanese]

- Mohamed AF, Matsumoto K, Tabata K, Takayama H, Kitajima M, Watanabe H. Effects of *Uncaria tomentosa* total alkaloid and its components on experimental amnesia in mice: elucidation using the passive avoidance test. *The Journal of Pharmacology and Pharmacy* 2000, 52(12): 1553-1561
- Moreno SR, Silva AL, Dire G, Honeycut H, Carvalho JJ, Nascimento AL, *et al.* Effect of oral ingestion of an extract of the herb *Uncaria tomentosa* on the biodistribution of sodium pertechnetate in rats. *Brazilian Journal of Medical and Biological Research* 2007, 40(1):77-80
- Mur E, Hartig F, Eibl G Schirmer M. Randomized Double Blind Trial of an extract from the Pentacyclic Alkaloid-Chemotype of *Uncaria tomentosa* for the Treatment of Rheumatoid Arthritis. *The Journal of Rheumatology* 2002, 29: 678-81
- Nogueira Neto J, Cavalcante FL, Carvalho RA, Rodrigues TG, Xavier MS, Furtado PG *et al.* Contraceptive effect of *Uncaria tomentosa* (cat's claw) in rats with experimental endometriosis. *Acta Cirúrgica Brasileira* 2011a, 26(2):s15-s19
- Nogueira Neto J, Coelho TM, Aguiar GC, Carvalho LR, Araújo AG, Girão MJ *et al.* Experimental endometriosis reduction in rats treated with *Uncaria tomentosa* (cat's claw) extract. *European Journal of Obstetrics Gynecology* 2011b, 154(2):205-208
- Nowakowska J, Sommer WA, Czubaj A, Kurae M, Skopinska-Rózewska E. The *in vitro* effect of *Uncaria tomentosa* and ethanol extract on the metabolic of blood granulocytes in mice. *Central European Journal of Immunology* 2010, 35(2):69-72
- Paniagua-Perez R, Madrigal-Bujaidar E, Molina-Jasso D, Reyes-Cadena S, Alvarez-Gonzalez I, Sanchez-Chapul L, *et al.* Antigenotoxic, antioxidant and lymphocyte induction effects produced by pteropodine. *Basic and Clinical Pharmacology and Toxicology* 2009, 104(3):222-227
- Pilarski R, Bednarczyk M, Gulewicz K. Evaluation of biological activity of *Uncaria tomentosa* (Willd.) DC. using the chicken embryo model. *Folia Biologica* 2009, 57(3-4):207-212
- Pilarski R, Filip B, Wietrzyk J, Kuras M, Gulewicz K. Anticancer activity of the *Uncaria tomentosa* (Willd.) DC. preparations with different oxindole alkaloid composition. *Phytomedicine* 2010, 17(14): 1133–1139
- Piscoya J, Rodriguez Z, Bustamante SA, Okuhama NN, Miller MJ, Sandoval M. Efficacy and safety of freeze-dried cat's claw in osteoarthritis of the knee: mechanisms of action of the species *Uncaria guianensis*. *Inflammation Research* 2001, 50(9):442-448
- Prado E, Garcia Gimenez MD, De la Puerta Vazquez R, Espartero Sanchez JL, Saenz Rodriguez MT. Antiproliferative effects of mitraphylline, a pentacyclic oxindole alkaloid of *Uncaria tomentosa* on human glioma and neuroblastoma cell lines. *Phytomedicine* 2007, 14(4):280-284
- Quílez AM, Saenz MT, Garcia MD. *Uncaria tomentosa* (Willd. ex. Roem. & Schult.) DC. and Eucalyptus globulus Labill. interactions when administered with diazepam. *Phytotherapy Research* 2012, 26(3):458-461
- Quinn J, Kaye J, Montine T, Stackman R. Phytochemicals in Alzheimer Disease: The Development of Clinical Trials. *Pharmaceutical Biology* 2004, 42(S1):64–73
- Rain-tree Tropical Plant database, *Uncaria tomentosa*, Cat's Claw. The text has been printed from "The Healing Power of Rainforest Herbs" by Leslie Taylor, copyrighted © 2004. Available at: <http://www.rain-tree.com/catclaw.htm#.VORsSfmG-FW>. Accessed 09/20/2014

- Ranilla LG, Kwon YI, Apostolidis E, Shetty K. Phenolic compounds, antioxidant activity and *in vitro* inhibitory potential against key enzymes relevant for hyperglycemia and hypertension of commonly used medicinal plants, herbs and spices in Latin America. *Bioresource Technology* 2010, 101(12):4676-4689
- Reinhard KH. *Uncaria tomentosa* (Willd.) D.C Cat's Claw, Una de Gato or Savéntero. *The Journal of Alternative and Complementary Medicine* 1999, 2:143-151
- Reis SR, Valente LM, Sampaio AL, Siani AC, Gandini M, Azeredo EL, *et al.* Immunomodulating and antiviral activities of *Uncaria tomentosa* on human monocytes infected with Dengue Virus-2. *International Immunopharmacology* 2008, 8(3):468-476
- Rizzi R, Re F, Bianchi A, De Feo V, de Simone F, Bianchi L *et al.* Mutagenic and antimutagenic activities of *Uncaria tomentosa* and its extracts. *Journal of Ethnopharmacology* 1993, 38(1):63-77
- Rojas-Duran R, Gonzalez-Aspajo G, Ruiz-Martel C, Bourdy G, Doroteo-Ortega VH, Alban-Castillo J, *et al.* Anti-inflammatory activity of Mitraphylline isolated from *Uncaria tomentosa* bark. *Journal of Ethnopharmacology* 2012, 143(3):801-804
- Romero-Jimenez M, Campos-Sanchez J, Analla M, Munoz-Serrano A, Alonso-Moraga A. Genotoxicity and anti-genotoxicity of some traditional medicinal herbs. *Mutation Research* 2005, 585(1-2):147-155
- Rotblatt M, Ziment I, editors. Evidence-based herbal medicine Hanley & Belfus, 2002 Philadelphia, PA, USA
- Roth I, Lindorf H, editors. South American Medicinal Plants. Springer-Verlag, Heidelberg 2002
- Sakakibara I, Terabayashi S, Kubo M, Higuchi M, Komatsu Y, Okada M, Taki K, Kamei J. Effect on locomotion of indole alkaloids from the hooks of *Uncaria* plants. *Phytomedicine* 1999, 6(3):163-168
- Salazar EL, Jayme V. Depletion of Specific Binding Sites for Estrogen Receptor by *Uncaria tomentosa*. *Proceedings of the Western Pharmacology Society* 1998, 41:123-124
- Sandoval-Chacón M, Thompson JH, Zhang XJ, Liu X, Mannick EE, Sadowska-Krowicka H *et al.* Antiinflammatory actions of cat's claw: the role of NF-kappaB. *Alimentary Pharmacology and Therapeutics* 1998, 12(2):1279-89
- Sandoval M, Chardonnet RM, Okuhama NN, Roberts J, Krenova Z, Trentacosti AM *et al.* Cat's claw inhibits TNF $\alpha$  production and scavenges free radicals role: in cytoprotection. *Free Radical Biology and Medicine* 2000, 29(1):71-78
- Sandoval M, Okuhama NN, Zhang XJ, Condezo LA, Lao J, Angeles' FM, *et al.* Anti-inflammatory and antioxidant activities of cat's claw (*Uncaria tomentosa* and *Uncaria guianensis*) are independent of their alkaloid content. *Phytomedicine* 2002, 9(4):325-337
- Santa Maria A, Lopez A, Diaz MM, Albán J, Galán de Mera A, Vicente Orellana JA, *et al.* Evaluation of the toxicity of *Uncaria tomentosa* by bioassays *in vitro*. *Journal of Ethnopharmacology* 1997, 57(3):183-187
- Sheng Y, Akesson C, Holmgren K, Bryngelsson C, Giamapa V, Pero RW. An active ingredient of Cat's Claw water extracts identification and efficacy of quinic acid. *Journal of Ethnopharmacology* 2005, 96(3):577-584



- Sheng Y, Bryngelsson C, Pero RW. Enhanced DNA repair, immune function and reduced toxicity of C-MED-100™, a novel aqueous extract from *Uncaria tomentosa*. *Journal of Ethnopharmacology* 2000a, 69(2): 115–126
- Sheng Y, Li L, Holmgren K, Pero R.W. DNA repair enhancement of aqueous extracts of *Uncaria tomentosa* in a human volunteer study. *Phytomedicine* 2001, 8(4):275–282
- Sheng Y, Pero RW, Wagner H. Treatment of chemotherapy-induced leukopenia in a rat model with aqueous extract from *Uncaria tomentosa*. *Phytomedicine* 2000b, 7(2):137-143
- Shi JS, Liu GX, Wu Q, Zhang XD, Huang XN. [Hypotensive and haemodynamic effects of isorhynchophylline in conscious rats and anesthetized dogs.] *Chinese Journal of Pharmacology and Toxicology* 1989, 3:205-210 [Chinese]
- Shi JS, Liu GX, Wu Q, Huang YP, Zhang XD. [Effects of rynchophylline and isorhynchophylline on blood pressure and blood flow of organs in anesthetized sized dogs.] *Acta Pharmacologica Sinica* 1992, 13(1):35-38 [Chinese]
- Shi JS, Huang B, Wu Q, Ren RX, Xie XL. Effects of rhynchophylline on motor activity of mice and serotonin and dopamine in rat brain. *Acta Pharmacologica Sinica* 1993, 14(2):114-117
- Shi ZH, Xi ZW, Wang H, Guan P, Yu P, Chang YZ, *et al.* The Neuroprotective Effect of Batch-2, an Aqueous Extract From Cat's Claw (*Uncaria tomentosa*) on 6-OHDA-Induced SH-SY5Y Cell Damage. *Progress in Biochemistry and Biophysics* 2010, 37(7):769-778
- Shi Z, Lu Z, Zhao Y, Wang Y, Zhao-Wilson X, Guan P, *et al.* Neuroprotective effects of aqueous extracts of *Uncaria tomentosa*: Insights from 6-OHDA induced cell damage and transgenic *Caenorhabditis elegans* model. *Neurochemistry International* 2013, 62(7):940-947
- Shimada Y, Goto H, Itoh T, Sakakibara I, Kubo M, Sasaki H, Terasawa K. Evaluation of the protective effects of alkaloids isolated from the hooks and stems of *Uncaria sinensis* on the glutamate-induced neuronal death in cultured cerebellar granule cells from rats. *Journal of Pharmacy in Pharmacology* 1999, 51(6):715-722
- Snow AD, Choi PY, Cummings JA, Wood S, Kirschner DA, Castillo GM. Isolation and testing of the amyloid-inhibiting ingredients derived from the natural beta-amyloid protein fibrillogenesis inhibitor PTI-00703. *Society For Neuroscience Abstracts* 2000, 26(1-2):Abstract No.299.3
- Snow AD, Rockenstein E, Cummings JA, Castillo GM, Choi PY, Masliah E. PTI-777 treatment causes a potent reduction of amyloid plaque burden in a transgenic mouse model of Alzheimer's disease. *Society For Neuroscience Abstracts* 2001, 127(2):Abstract No.1806
- Styczynski J, Wysocki M. Alternative medicine remedies might stimulate viability of leukemic cells. *Pediatric Blood and Cancer* 2006, 46(1):94-98
- Taylor L. *Herbal Secrets of the Rainforests* 2<sup>nd</sup> ed. Sage Press, Inc., Austin, TX, USA 2002
- USP 37 The United States Pharmacopeia, NF 32 The National Formulary, Dietary Supplements. Cat's Claw, Powdered Cat's Claw, Powdered cat's Claw Extract, Cat's Claw Capsules, Cat's Claw Tablets, The United States Pharmacopeial Convention, Rockville, MD, 2014, 5295-5303
- Valerio LG Jr, Gonzales GF. Toxicological Aspects of the South American Herbs Cat's Claw (*Uncaria tomentosa*) and Maca (*Lepidium meyenii*). A Critical synopsis. *Toxicological Reviews* 2005, 24(1):11-35

- Vattimo NMFF, da Silva NO. *Uncaria tomentosa* and acute ischemic kidney injury in rats. *Revista da Escola de Enfermagem da USP* 2011, 45(1):189-93
- Vogel JH, Bolling SF, Costello RB, Guarneri EM, Krucoff MW, Longhurst JC, *et al.* Integrating complementary medicine into cardiovascular medicine. A report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents (Writing Committee to Develop an Expert Consensus Document on Complementary and Integrative Medicine). *Journal of the American College of Cardiology* 2005, 46(1):184-221
- Wagner H, Kreutzkamp B, Jurcic K. Die Alkaloide von *Uncaria tomentosa* und ihre Phagozytose-steigernde Wirkung. *Planta Medica* 1985, 51(5):419-423 [German]
- White G, Bourbonnais-Spear N, Garner F. Antibacterial constituents from *Uncaria tomentosa*. *Phytopharmacology* 2011, 1(2):6-19
- WHO monographs on selected medicinal plants. Vol. 3. Cortex *Uncariae*. World Health Organization. Geneva 2007, 349-358
- Winkler C, Wirleitner B, Schroecksadel K, Schennach H, Mur E, Fuchs D. *In vitro* effects of two extracts and two pure alkaloid preparations of *Uncaria tomentosa* on peripheral blood mononuclear cells. *Planta Medica* 2004, 70(3):205-210
- Wirth C, Wagner H. Pharmacologically active procyanidines from the bark of *Uncaria tomentosa*. *Phytomedicine* 1997, 4(3):265-266
- Wurm M, Kacani L, Laus G, Keplinger K, Dierich MP. Pentacyclic oxindole alkaloids from *Uncaria tomentosa* induce human endothelial cells to release a lymphocyte-proliferation-regulating factor. *Planta Medica* 1998, 64(8):701-704
- Yamahara J, Miki S, Matsuda H, Kobayashi G, Fujimura H. [Screening test for calcium antagonist in natural products. The active principles of *Uncariae ramulus et uncus*.] *Nihon Yakurigaku Zasshi* 1987, 90(3):133-139 [Japanese]
- Yano S, Horiuchi H, Horie S, Aimi N, Sakai S, Watanabe K. Ca<sup>2+</sup> Channel Blocking Effects of Hirsutine, an Indole Alkaloid from *Uncaria* Genus, in the Isolated Rat Aorta. *Planta Medica* 1991, 57(5):403-405
- Zhang W, Liu GX, Huang XN. [Effect of rhynchophylline on contraction of rabbit aorta.] *Acta Pharmacologica Sinica* 1987, 8(5):425-429 [Chinese]
- Zhang L, Zhang J, Zhao B, Zhao-Wilson X. Quinic acid could be a potential rejuvenating natural compound by improving survival of *Caenorhabditis elegans* under deleterious conditions. *Rejuvenation Research* 2012, 15(6):573-583
- Zhu Y, Huang X, Liu G. [Effects of isorhynchophylline on physiological characteristics of isolated guinea pig atrium.] *Zhongguo Zhong Yao Za Zhi* 1995, 20(2):112-4 [Chinese]

## References assessed, but not cited in the assessment report:

- Amaral S, Mira L, Nogueira JM, da Silva AP, Helena Florencio M. Plant extracts with anti-inflammatory properties--a new approach for characterization of their bioactive compounds and establishment of structure-antioxidant activity relationships. *Bioorganic and Medicinal Chemistry* 2009, 17(5):1876-1883
- Bacher N, Tiefenthaler M, Sturm S, Stuppner H, Ausseriechner MJ, Kofler R *et al.* Oxindole alkaloids from *Uncaria tomentosa* induce apoptosis in proliferating, G0/G1-arrested and bcl-2-expressing acute lymphoblastic leukaemia cells. *British Journal of Haematology* 2006, 132(5):615-22
- Ccahuana-Vasquez RA, dos Santos SSF, Koga-Ito CY, Jorge AOC. Antimicrobial activity of *Uncaria tomentosa* against oral human pathogens. *Brazilian Oral Research* 2007, 21(1):46-50
- Choi HR, Choi JS, Han YN, Bae SJ, Chung HY. Peroxynitrite scavenging activity of herb extracts. *Phytotherapy Research* 2002, 16(4):364-367
- Garcia EJ, Oldoni TL, Alencar SM, Reis A, Loguercio AD, Grande RH. Antioxidant activity by DPPH assay of potential solutions to be applied on bleached teeth. *Brazilian Dental Journal* 2012, 23(1):2-27
- Herrera DR, Tay LY, Rezende EC, Kozlowski VA Jr, dos Santos EB. *In vitro* antimicrobial activity of phytotherapeutic *Uncaria tomentosa* against endodontic pathogens. *Journal of Oral Science* 2010, 52(3):473-6
- Kaiser S, Dietrich F, de Resende PE, Verza SG, Moraes RC, Morrone FB, *et al.* Cat's claw oxindole alkaloid isomerization induced by cell incubation and cytotoxic activity against T24 and RT4 human bladder cancer cell lines. *Planta Medica* 2013, 79(15):1413-1420
- Kuras M, Pilarski R, Nowakowska J, Zobel A, Brzost K, Antosiewicz J, *et al.* Effect of Alkaloid-Free and Alkaloid-Rich preparations from *Uncaria tomentosa* bark on mitotic activity and chromosome morphology evaluated by Allium Test. *Journal of Ethnopharmacology* 2009, 121(1):140-147
- Mazzio E. A., Soliman K. F. *In vitro* screening for the tumoricidal properties of international medicinal herbs. *Phytotherapy Research* 2009, 23(3):385-398
- Muhammad I, Dunbar DC, Khan RA, Ganzera M, Khan IA. Investigation of Uña De Gato I. 7-Deoxyloganic acid and <sup>15</sup>NMR spectroscopic studies on pentacyclic oxindole alkaloids from *Uncaria tomentosa*. *Phytochemistry* 2001, 57(5):781-785
- Ostrakhovich EA, Mikhalchik EV, Getmanskaya NV, Durnev AD. Antioxidant activity of the extract from *Uncaria Tomentosa*. *Pharmaceutical Chemistry Journal* 1997, 31(6):326-329
- Ostrakhovich EA, Getmanskaya NV, Durnev AD. Effects of *Uncaria Tomentosa* extract on peroxynitrite production by polymorphonuclear leukocytes of peripheral blood in healthy donors and diabetes mellitus patients. *Pharmaceutical Chemistry Journal* 1998, 32(10):543-545
- Pilarski R, Poczekaj-Kostrzewska M, Ciesiolka D, Szyfter K, Gulewicz K. Antiproliferative activity of various *Uncaria tomentosa* preparations on HL-60 promyelocytic leukemia cells. *Pharmacological Report* 2007, 59(5):565-572
- Pilarski R, Zieliński H, Ciesiołka D, Gulewicz K. Antioxidant activity of ethanolic and aqueous extracts of *Uncaria tomentosa* (Willd.) DC. *Journal of Ethnopharmacology* 2006, 104(1-2):18-23

Rain-tree Tropical Plant database, The Cat's Claw TOA / POA Controversy, Last updated 12-29-2012  
<http://www.rain-tree.com/toa-poa-article.htm>

Rinner B, Li ZX, Haas H, Siegl V, Sturm S, Stuppner H, *et al.* Antiproliferative and pro-apoptotic effects of *Uncaria tomentosa* in human medullary thyroid carcinoma cells. *Anticancer Research* 2009, 29(11):4519-4528

Riva L, Coradini D, Di Fronzo G, De Feo V, De Tommasi N, De Simone F, *et al.* The antiproliferative effects of *Uncaria tomentosa* extracts and fractions on the growth of breast cancer cell line. *Anticancer Research* 2001, 21(4A):2457-2461

Sheng Y, Pero RW, Amiri A, Bryngelsson C. Induction of apoptosis and inhibition of proliferation in human tumor cells treated with extracts of *Uncaria tomentosa*. *Anticancer Research* 1998, 18(5A):3363-3368

Stuppner H, Sturm S, Geisen G, Zillian U, Konwalinka G. A differential sensitivity of oxindole alkaloids to normal and leukemic cell lines. *Planta Medica* 1993, 59:A583