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Efficacy and safety of freeze-dried cat's claw in osteoarthritis of the knee: mechanisms of action of the species *Uncaria guianensis*

J. Piscoya [1], Z. Rodriguez [1], S.A. Bustamante [2], N. N. Okuhama [3], M.J.S. Miller [3] and M. Sandoval [3]

[1] Universidad Nacional Mayor de San Marcos, Facultad de Medicina, Lima, Peru

[2] Rainforest Phytoceuticals, LLC, Delmar, NY, USA

[3] Center for Cardiovascular Sciences, Albany Medical College, 47 New Scotland Avenue (MC8), Albany, NY, 12208, USA, Fax: ++518 262 5241, e-mail: sandovm@mail.amc.edu

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Abstract. *Aim:* The purpose of this investigation was to evaluate the ability of cat's claw, an Amazonian medicinal plant, to treat osteoarthritis of the knee, collect safety and tolerance information and compare the antioxidant, and anti-inflammatory actions of *Uncaria guianensis* and *Uncaria tomentosa* in vitro.
Materials and methods: Forty-five patients with osteoarthritis of the knee were recruited, 30 were treated with freeze-dried *U. guianensis*, and 15 with placebo. Hematological parameters were assessed on entry and exit of the four-week trial. Pain, medical and subject assessment scores and adverse effects were collected at weeks 1, 2 and 4. The antioxidant and anti-inflammatory activity of the cat's claw species was determined by the α,α-diphenyl-β-picrylhydrazyl (DPPH) free radical scavenging method. Inhibition of TNFα and prostaglandin E_2 (PGE_2) production was determined in RAW 264.7 cells by ELISA.
Results: Cat's claw had no deleterious effects on blood or liver function or other significant side-effects compared to placebo. Pain associated with activity, medical and patient assessment scores were all significantly reduced, with benefits occurring within the first week of therapy. Knee pain at rest or at night, and knee circumference were not significantly reduced by cat's claw during this brief trial. In vitro tests indicated that *U. guianensis* and *U. tomentosa* were equivalent at quenching DPPH radicals (EC_{50}, 13.6–21.7 µg/ml) as well as inhibiting TNFα production. However, the latter action was registered at much lower concentrations (EC_{50}, 10.2–10.9 ng/ml). Cat's claw (10 µg/ml) had no effect on basal PGE_2 production, but reduced LPS-induced PGE_2 release ($P < 0.05$), but at higher concentrations than that required for TNFα inhibition.
Conclusion: Cat's claw is an effective treatment for osteoarthritis. The species, *U. guianensis* and *U. tomentosa* are equiactive. They are effective antioxidants, but their anti-inflammatory properties may result from their ability to inhibit TNFα and to a lesser extent PGE_2 production.

Key words: Inflammation – TNFα – Antioxidant – Prostaglandin – Complimentary medicine

Introduction

Cat's claw is a medicinal plant from the Amazon River basin that has been used for the treatment of chronic inflammation, including arthritis, by indigenous cultures for centuries. Despite its increasing popularity in the Western world, there are no studies that have assessed its therapeutic potential for arthritis in a placebo controlled trial. This present investigation was designed to assess this potential, and in addition, compare the antioxidant and anti-inflammatory properties of two species of cat's claw. In the Western world *Uncaria tomentosa* is better known than *Uncaria guianensis*, but both species share the same traditional ethnomedical applications. To date a direct comparison of these species in models of inflammation is lacking.

Preclinical evaluation of cat's claw has largely been directed at *Uncaria tomentosa*. We have described that this specie of cat's claw protects against a multitude of oxidative stresses, including peroxynitrite [1] which has been implicated as a mediator of arthritis [2] and other chronic inflammatory disorders [3, 4], as well as UV radiation and free radical (α,α-diphenyl-β-picrylhydrazyl, DPPH) induced cytotoxicity [5]. Further, we have observed that cat's claw prevents the gastrointestinal damage from high dose NSAIDs, either as acute gastritis [6] or chronic enteritis [5]. These observations alone would suggest that cat's claw be considered as an adjunct therapy in the treatment of arthritis. However, as cat's claw may attenuate directly arthritic joint pain and dysfunc-

Correspondence to: M. Sandoval

tion a detailed assessment in arthritis is warranted. Previously, many have erroneously considered cat's claw as an immune stimulant, a counter-intuitive concept for an anti-inflammatory agent that arose from a patent on the oxindole alkaloids present in Cat's claw [7–9]. We have described that cat's claw is a remarkably potent inhibitor of NF-κB [1], a critical transcription factor implicated in arthritis [10, 11]. Inhibition of NF-κB is a highly prized mechanism in the development of new anti-inflammatory agents. We have determined that cat's claw (*Uncaria tomentosa*) is an effective inhibitor of TNFα gene expression in vitro and in vivo. TNFα production is regulated at the transcriptional level, largely by NF-κB [11]. The effectiveness of TNFα antibody therapies for arthritis is proof positive that NF-κB activation and TNFα production are critical elements of the disease process [12, 13]. Consequently, any therapeutic agent that shares this action has the potential to offer benefit in arthritis [14]. In addition, considering that osteoarthritis (OA) is the most common form of arthritis in developing countries and the United States [15], and causes pain and disability in older people [16–18], it is warranted to investigate the use of this Amazonian medicinal plant for the treatment of OA. To test this hypothesis, we set out to evaluate a cat's claw specie, *Uncaria guianensis* in osteoarthritis a specie low in oxindole alkaloids, and to compare its in vitro actions with *Uncaria tomentosa*.

Materials and methods

Materials

Except where noted, all chemicals were at least reagent grade and were obtained from Sigma Chemical Company (St. Louis, MO). Cat's claw (*Uncaria tomentosa* and *Uncaria guianensis*) was collected from the Upper Tropical Region of Peru. The authenticity of the two species of cat's claw was confirmed by Ing. Warren Rios, Professor at Universidad Nacional Agraria de la Selva, Tingo Maria, Peru.

Cat's claw preparation

For the clinical trial, an aqueous extraction of cat's claw bark (*Uncaria guianensis*) was prepared by boiling in hot water for 30 minutes, decanted and total solids separated by filtration with a Whatman N° 4 filter paper. The filtrate was then freeze-dried in the laboratories of Universidad Nacional Mayor de San Marcos, Lima, Peru. Then tablets were prepared with the freeze-dried (100 mg + excipient). For the in vitro experiments, Rainforest Phytoceuticals, LLC (Delmar, NY, www.amazon-medicines.com), supplied purified freeze-dried extracts of *Uncaria tomentosa* and *Uncaria guianensis*.

Patients

Forty-five male patients, ages 45-75 years, with symptomatic osteoarthritis (OA) of the knee (grades II-III of the Kellgren/Lawrence (K/L) classification [19], fulfilling the American College of Rheumatology criteria for the knee [20], and with pain present most days of the prior month were recruited for the study. Radiographic evidence of knee OA was defined by the presence of osteophytes in at least 1 tibiofemoral compartment. Criteria for entry into the study were osteoarthritis of the knee that required NSAID therapy for at least 3 months prior to the study, and there had to be evidence of knee pain on movement scored by the patient [21]. Before entering the trial, patients underwent washout periods of 7 days for any NSAIDs or 12 hours for analgesics. During the trial, acetaminophen intake (500-mg tablets) was permitted in cases of persistent pain, and the dose and duration were recorded. Entry also required a normal liver and hematological function assessment (alanine aminotransferase – ALT; aspartate aminotransferase – AST; erythrocyte sedimentation rate – ESR, hematocrit and hemoglobin) at baseline as previously described [22].

Patients were not retained for the study if they had serious concomitant medical illness (pre-existing renal, cardiovascular, gastrointestinal, hepatic or hematological complications, and history of alcoholism or drug abuse), secondary OA, radiographic grade IV by the K/L classification, hypersensitivity reactions to salicylates nor patients taking oral anticoagulants, systemic or treated with intraarticular injection of glucocorticoids for at least three months before the study.

Study design

This was a prospective, multicenter, randomized, double blind, placebo-controlled, parallel trial of 4-week duration. This duration was chosen according to personal communication from previous patients taking freeze-dried cat's claw, and also to gain more information about cat's claw safety profile. The study was conducted in accordance with the Helsinki Declaration (1964) and its revision (1975). Patients entered the study after fulfilling the inclusion and exclusion criteria and signing an informed consent.

Cat's claw administration

Patients were randomly assigned to two treatment groups. One group (n = 15) received placebo (1 capsule daily), the second group (n = 30) received 100 mg of freeze-dried cat's claw (1 capsule of 100 mg daily). Placebo tablets contained the same excipient but without cat's claw. Physicians and patients were blind to the treatment nature, and identical procedures were also used in the laboratory analysis.

Evaluation of efficacy

Subjects were assessed at the commencement of the study for pain at rest, at night and during exercise. Tenderness was scored on a 4-point scale [21], (0 = no tenderness, 1 = patient complained of pain, 2 = patient complained of pain and winced, 3 = patient complained of pain, winced and withdrew the joint). The global tolerance to the study treatment was assessed by the patient and the investigator at weeks 1–4 of the trial, as described previously [23–25] with a scoring system using a 5-point scale (very good, good, moderate bad and very bad). Subjects were also assessed at the conclusion of the study for ALT, AST, ESR, hematocrit and hemoglobin. All adverse effects (AEs) reported by the patients during the study treatment were recorded on the case report form (CRF) and described their nature, frequency and severity.

Free radical scavenging assay.

The DPPH free radical scavenging method previously reported [26] was modified as follows. The soluble solids content of the cat's claw extracts were standardized to give stock solutions containing 20 mg/ml water. An aliquot of the freeze-dried cat's claw extracts (*U. tomentosa* or *U. guianensis*) were placed in a cuvette and a 60 µM ethanolic solution of DPPH were added (final vol 1 ml). The decrease in absorbance at 515 nm was determined continuously with data capturing at 30-sec intervals with a Beckman Coulter DU-640 spectrophotometer (Beckman Instruments, Fullerton, CA). All determinations were performed in triplicate. The DPPH scavenging capacity of cat's claw was determined as previously described [5]. Ascorbic acid (10–100 µM) was used as a reference antioxidant-control to compare the efficacy of DPPH inhibition.

Inhibition of TNFα production

The ability of cat's claw to inhibit TNFα synthesis/release in vitro was determined by stimulating TNFα production in RAW 264.7 cells (1×10^5 cells/well), a murine macrophage cell line, after administration of lipopolysaccharide (LPS, 50 ng/ml). Cells were either pretreated with cat's claw (*Uncaria tomentosa or Uncaria guianensis*) with concentrations ranging from 1 to 1000 ng/ml for two h and/or treated with LPS (50 ng/ml) for 1 h. The media was then replaced and cells were incubated at 37 °C for 16 h. Culture medium was collected for determination of TNFα levels using the Quantikine M mouse TNFα Immunoassay kit (R & D Systems Inc., Minneapolis, MN). Samples were processed for ELISA determinations following the manufacturer's recommendations.

Inhibition of PGE_2 production

RAW 264.7 cells (1×10^6 cells/well) were used to determine the capacity of cat's claw (*Uncaria tomentosa*) to decrease the production of LPS-induced prostaglandin E_2 (PGE_2). Cells were pretreated with cat's claw (10 µg/ml) for 1 h, then the media was replaced with medium containing LPS (50 ng/ml), and cells were incubated at 37 °C for 4 h. At the end of the incubation period, medium was collected and PGE_2 was quantified using a Prostaglandin E_2 EIA kit-monoclonal (Cayman Chemical, Ann Arbor, MI).

Data analysis

Clinical trial data was evaluated by one-way ANOVA followed by post hoc analysis with the Kruskal-Wallis and Mann-Whitney test. Results are expressed as the mean ± SE. Statistical analysis for the in vitro experiments was performed using t-test and one-way ANOVA. Post hoc comparison of means was done by Least Significant Difference test and unpaired t-test. A probability value of < 0.05 was considered significant.

Results

Clinical Trial

At the commencement of the study there was no difference between the treatment groups in all variables assessed – hematological and disease activity scores, indicating effective randomization (Table 1). Compared to placebo, the cat's claw group had a significant improvement in the pain associated with activity (Fig. 1), patient and medical assessment scores (Fig. 2). Importantly, all of these indices were found to be improved significantly after one week of the trial, with the exception of the medical assessment score which bordered on significance ($P = 0.0715$) but improvement was highly significant at weeks 2 and 4 ($P < 0.001$). In addition, there was a significant improvement in these disease indices with time of treatment ($P < 0.05$), with scores at week 4 lower than baseline or week 1 values.

In contrast, pain at rest or at night, and knee circumference (Table 2) were not significantly altered in either placebo or cat's claw groups during the course of the study. No change in hematological determinations was observed in either group, over the course of the study (Table 3). There was also no difference in the incidence and form of side effects reported by the two groups. Specifically, at week one, in the cat's claw group one patient presented with vomiting

Table 1. Patient demographics and baseline characteristics.

	Placebo (n = 15)	100 mg/day Freeze-dried cat's claw (n = 30)
Age, years	60.9 ± 6.5	59.9 ± 8.4
Rest pain score	4.2 ± 2.9	4.4 ± 2.6
Activity pain score	6.8 ± 1.9	5.7 ± 2.6
Night pain score	4.6 ± 2.8	4.6 ± 2.3
Right knee perimeter	41.2 ± 8.4	39.0 ± 7.4
Left knee perimeter	40.0 ± 7.1	38.6 ± 8.4

Values are the mean ± SD. No statistical differences between the two groups.

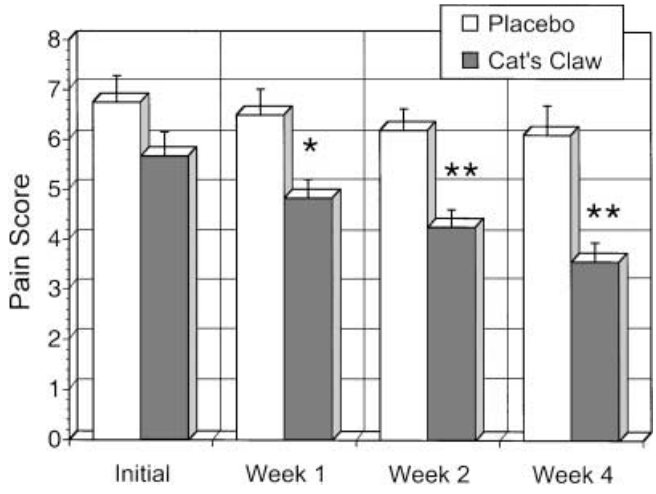

Fig. 1. Pain on activity scores in placebo (n = 15) and cat's claw (n = 30) treated groups at the commencement of the trial, as well as determinations at week 1, 2 and 4. The single * indicates significant difference from placebo ($P < 0.01$) and ** indicates significant difference from placebo ($P < 0.001$).

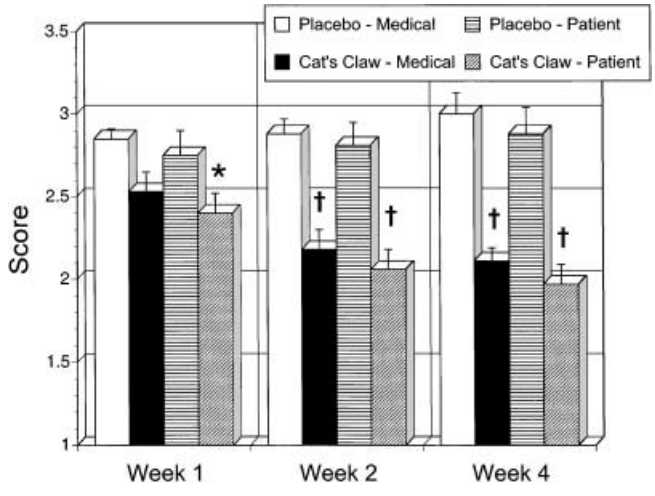

Fig. 2. Physician (medical) and patient assessment scores of disease activity in placebo (n = 15) and cat's claw (n = 30) treated groups, as determined at week 1, 2 and 4 of the trial. The * indicates a significant difference from placebo ($P < 0.05$), and the † indicates significant difference from placebo ($P < 0.001$).

Table 2. Effect of cat's claw (*Uncaria guianensis*) on measures of pain at rest and night.

Assessment of pain	Placebo		Freeze-dried cat's claw	
	Entry	Week 4	Entry	Week 4
Score at rest	4.15 ± 0.77	3.94 ± 0.69	4.41 ± 0.48	3.42 ± 0.33
Score at night	4.60 ± 0.74	4.17 ± 0.69	4.63 ± 0.42	3.06 ± 0.37

Values are mean ± SE from participants of the study.

Table 3. Effect of cat's claw (*Uncaria guianensis*) on hematological parameters.

Assessment	Placebo		Freeze-dried Cat's claw	
	Entry	Week 4	Entry	Week 4
Hemoglobin, g/dL	14.41 ± 2.01	12.67 ± 0.31	12.75 ± 0.23	13.89 ± 1.05
Hematocrit, %	37.29 ± 2.41	39.15 ± 1.29	38.00 ± 0.67	36.87 ± 1.30
ESR, mm/h	20.97 ± 1.49	16.56 ± 0.98	17.80 ± 1.08	17.75 ± 1.18
AST, U/L	32.82 ± 8.59	25.31 ± 2.17	21.77 ± 1.37	29.69 ± 8.11
ALT, U/L	19.41 ± 2.65	21.12 ± 2.08	21.04 ± 1.51	19.38 ± 1.63

Values are mean ± SE from participants of the study as described in materials and methods. Erythrocyte sedimentation rate (ESR), Aspartate aminotransferase (AST), and Alanine aminotransferase (ALT).

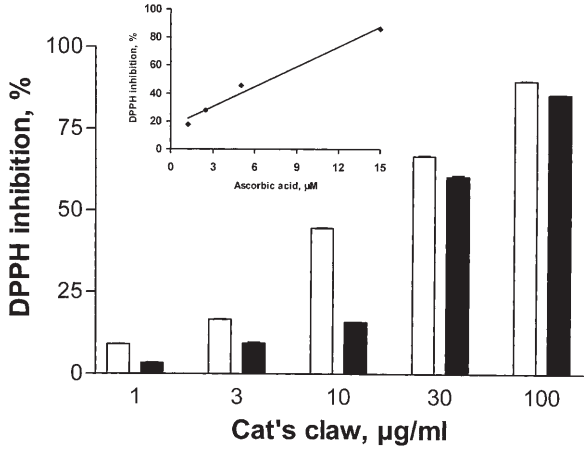

Fig. 3. Antioxidant activity of cat's claw assessed by DPPH free radical method. The DPPH scavenging capacity of cat's claw *Uncaria guianensis* (solid bars) and *Uncaria tomentosa* (open bars) was quantified spectrophotometrically at 515 nm. In vitro reactions were carried out for 5 min and the degree of DPPH inhibition is expressed as absorbance depletion as described in Materials and methods. Values are mean ± SE of three experiments with three samples each. No significant difference between the species was noted in their ability to quench DPPH. Inset: DPPH inhibition by ascorbic acid as antioxidant of reference r = 0.9784 (EC_{50}, 4.8 µM).

and another with dizziness. At week two, the cat's claw group had 5 patients reporting headache (P = 0.1526), and at week four, three patients in the cat's claw group and one patient in the placebo group presented with headache; one patient in the placebo group reported dizziness and another reported ringing in the ears (P = 0.3842).

Table 4. Comparison of the antioxidant and anti-TNFα activities of cat's claw species.

Assay	Freeze-dried cat's claw			
	Uncaria tomentosa		*Uncaria guianensis*	
	EC_{50}	Max Inhibition, %	EC_{50}	Max Inhibition, %
Antioxidant (DPPH)	21.7 µg/ml	85.5	13.6 µg/ml	90.5
Anti-TNFα	10.2 ng/ml	79.0	10.9 ng/ml	73.0

Freeze-dried cat's claw was used for these experiments. The antioxidant activity was assayed by in vitro scavenging of the free radical DPPH (60 µM), and quantified spectrophotometrically at 515 nm. The anti-TNFα activity was determined using the Quantikine M mouse TNFα immunoassay as described in Materials and methods.

Free radical scavenging

DPPH gives a steady absorbance reading at 515 nm. Absorbance declined in the presence of cat's claw (Fig. 3), indicating radical quenching. The effectiveness of *Uncaria guianensis* and *Uncaria tomentosa* as DPPH scavengers is shown in Figure 3. The EC_{50} for both species were 13.6 vs 21.7 µg/ml, respectively (Table 4). While the rate of quenching may have been marginally greater for *Uncaria guianensis* at some concentrations this had no impact on total antioxidant activity. Thus, we regard their antioxidant activity in this system to be comparable.

Inhibition of TNFα production

Murine macrophages (RAW 264.7 cells) when stimulated with LPS release substantial quantities of TNFα into the media. Inclusion of cat's claw into the media prior to LPS administration, resulted in a dose-dependent reduction in TNFα levels (Fig. 4, $P < 0.001$). As observed with the DPPH assay, the potency of *Uncaria tomentosa* and *Uncaria guianensis* extracts as inhibitors of TNFα synthesis were equivalent in this assay. It is important to note however that the concentrations required to inhibit TNFα production were considerably lower than that needed to quench DPPH radicals (Table 4).

Inhibition of PGE_2 production

Murine macrophages (RAW 264.7 cells) were also used to assess PGE_2 release. Cat's claw had no effect on basal (unstimulated) PGE_2 production, indicating that cyclooxygenase-1 (COX-1) activity was not influenced. However, the marked increase in PGE_2 production induced by LPS (0.5 µg/ml) was significantly reduced ($P < 0.05$) by cat's claw (Figure 5), suggestive of an inhibition of cyclooxygenase-2 (COX-2) expression. The dose of cat's claw (10 µg/ml) was greater than that required suppressing TNFα production but less than concentrations required for antioxidant activity.

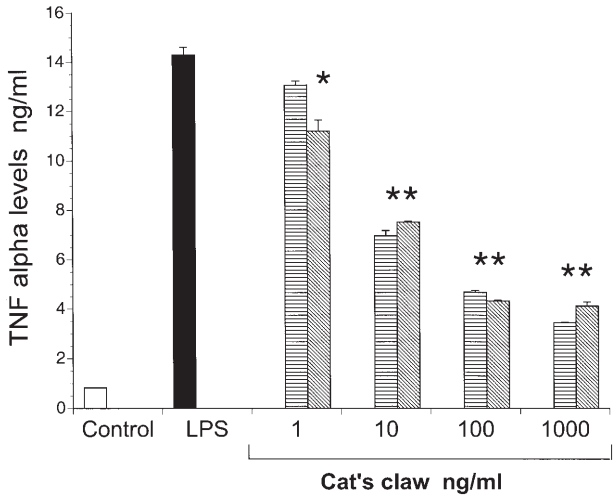

Fig. 4. Effect of cat's claw (*Uncaria tomentosa* and *Uncaria guianensis*) on LPS-induced TNFα production by macrophages (RAW 264.7). Cells were seeded at 1×10^5 cells/well. Freeze-dried concentrates from both species of cat's claw inhibited TNFα production in an equivalent dose-dependent manner. Bars represent TNFα release into the media for *Uncaria tomentosa* (horizontal) and *Uncaria guianensis* (cross). Cells were treated with LPS (50 ng/ml) for 1 h or pretreated with freeze-dried cat's claw for 2 h then challenged with LPS for 1 h, and incubated for 16 h as described in Materials and methods. All data represent mean ± SE for triplicate determinations. * significant decrease ($P < 0.05$) from LPS alone for *Uncaria guianensis*. ** significant decrease ($P < 0.01$) from LPS alone, for both species.

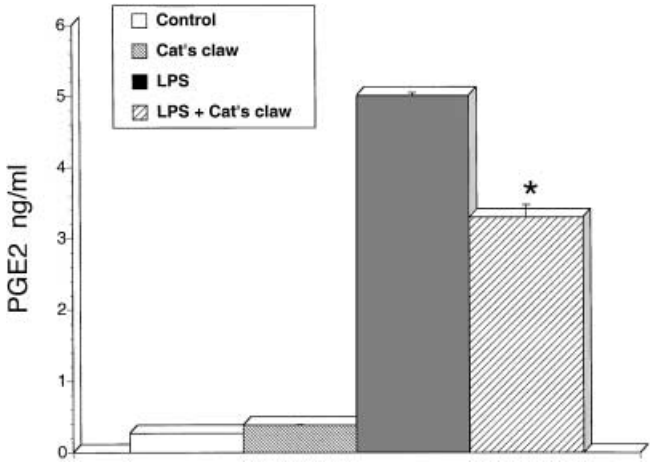

Fig. 5. Effect of cat's claw (*Uncaria tomentosa*) on prostaglandin E_2 (PGE_2) production. Murine macrophages (RAW 264.7 cells) were pretreated with cat's claw (10 µg/ml) for 1 h and/or treated with LPS (50 ng/ml) for 4 h. PGE_2 release into the media was assessed by ELISA as described in Materials and methods. All data represent mean ± SE for triplicate determinations. * significant decrease ($P < 0.05$) from LPS alone.

Discussion

This placebo-controlled double blind study clearly defines that cat's claw (*Uncaria guianensis*) is an effective treatment for osteoarthritis of the knee. Within the four-week study protocol the major benefits of cat's claw treatment were in alleviating pain associated with exercise, patient and physician assessment scores. Improvement in knee circumference and pain at rest or at night was not observed but this may reflect the duration of treatment, as therapeutic trends were evident with cat's claw and treatment duration was a significant factor in the disease assessment scores and pain with exercise. Cat's claw therapy was not associated with any changes in liver or hematological function, and the incidence and frequency of side effects was not different from placebo control. In this limited study we confirm the ethnomedical reputation of cat's claw for being well tolerated and safe.

Whether the more popular specie of cat's claw, *Uncaria tomentosa*, is more effective in treating arthritis is unknown and was not the goal of this study. However, we attempted to address this issue in the laboratory setting. *Uncaria tomentosa* and *Uncaria guianensis* displayed comparable antioxidant activity using the DPPH free radical scavenging assay. Certainly oxidative stress and free radical damage has been implicated in arthritis [27–29] and other chronic inflammatory diseases [3, 5]. The antioxidant function of cat's claw may explain its ability to offer benefit to patients with osteoarthritis. On the other hand, the therapeutic benefits of antioxidants alone can be questioned.

In the TNFα production assay, species were equivalent, producing substantial reductions in TNFα synthesis. A critical finding was that suppression of TNFα production was noted at concentrations that were far less than that required for antioxidant activity (Table 4). The cytokine TNFα is regarded as a critical mediator of chronic inflammation [30, 31], including arthritis [13, 14, 32]. The success of Inflximab™, the TNFα antibody therapy in bringing active disease into quiescence is proof positive that TNFα is a legitimate therapeutic target. Whether the benefits of cat's claw are solely due to inhibition of TNFα production is unknown. Indeed, the use of TNFα antibody therapy is usually confined to rheumatoid arthritis and here we have examined the effects of cat's claw in osteoarthritis. However, inflammatory mediators are activated in both forms of joint inflammation although differences in cellular source and etiology exist [33]. We have demonstrated that cat's claw inhibits TNFα gene expression in gastric mucosa in NSAID gastritis [6]: an action that is the result of its ability to inhibit the activation of NF-κB [1]. The transcription factor NF-κB, is a redox-sensitive transcription factor that regulates the expression of over 28 different genes involved in inflammation [12], coordinating many aspects of the inflammatory process (adhesion molecules, cytokines, chemokines, enzymes). Inducible nitric oxide synthase is an example of a NF-κB regulated gene, that has been implicated in osteoarthritis [28, 29], whose expression can be reduced by either cat's claw directly [1] or by anti-TNFα antibody [32]. Thus, suppression of NF-κB activation is critical target for treating inflammation, as has been demonstrated with antisense technology [34]. While NF-κB is activated by oxidants, there was a clear discrepancy in the concentrations required for these two species, *Uncaria tomentosa* and *Uncaria guianensis* to act either as antioxidants or anti-TNFα agents. We interpret this to mean that the different constituents in this decoction are responsible for antioxidant and anti-TNFα activities, or alternatively these components are functionally more directed at transcriptional inhibition than antioxidant activity.

The importance of this study is that it provides therapeutic information as to the application of a medicinal plant in

the treatment of osteoarthritis. This type of information, along with safety and tolerability data, will assist health care professionals to make informed and educated decisions as to the utility of cat's claw. It should be noted that this freeze-dried formulation was quite potent. Dosing at 100 mg once a day reflects a potency that one normally associates with a pharmaceutical rather than a medicinal plant preparation. On the other hand, we have determined that the micropulverization preparative method, which is the standard formulation in the Western world, is approximately 20-fold less potent [5], in which case gram quantities will be needed to achieve the same effects.

Cat's claw has had enjoyed a remarkable clinical experience in South America, and it is highly regarded for the treatment of chronic inflammation [35]. This study as well as our previous investigations [1, 5, 6], supports this ideology. Of particular interest in the treatment of arthritis is the ability of cat's claw to not only confer benefit to the joints but also negate the side effects of NSAIDs on the stomach and intestine [5, 6]. With the observation that cat's claw significantly lowered PGE_2 production by macrophages, presumably due to an inhibition of COX-2 expression, concomitant with in vivo benefits on pain, it is likely that cat's claw administration may lower the need for arthritic patients to consume NSAIDs. Thus, this Amazonian botanical not only treats the arthritic disease process but also reduces the toxic side effects of the current standard pharmaceuticals used in the management of arthritis. The concept that botanicals can be used to reduce the toxicity of pharmaceuticals is an intriguing and greatly under-explored area of investigation.

Another complimentary medicine approach to osteoarthritis that is more commonly appreciated is the use of glucosamine and chondroitin sulfate [36]. While the mechanisms of action of these nutraceuticals have not been completely elucidated [37], their actions appear to be quite distinct from cat's claw. Glucosamine and chondroitin are substrates for cartilage and as such, assist in replacing chondrocyte material that is lost during the inflammatory process. There is no evidence for a direct action on gene expression or antioxidant activity, in contrast to the present observations with cat's claw. Thus, it is clear that this disease can be approached therapeutically from different perspectives. However, we believe that an approach that directly interrupts the disease process has a better chance for therapeutic benefits in a large proportion of the population than an approach that is designed to arithmetically replace substrates lost as a result of ongoing inflammation. In that regards, cat's claw is also distinct from NSAIDs as they only treat the symptoms of the condition (pain, swelling) and not the underlying disease process. Given the ability of cat's claw to negate the side effects of NSAIDs, it is possible that a combination of cat's claw and NSAID would be a significant improvement in the management of arthritis, and a cost-effective alternative to COX-2 inhibitors.

We conclude that cat's claw is a medicinal plant that deserves further consideration in the treatment of arthritis and other chronic inflammatory disorders.

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