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Cat's claw: An Amazonian vine decreases inflammation in osteoarthritis

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Summary Cat's claw (*Uncaria tomentosa* and *Uncaria guianesis*) is a medicinal plant from the Amazon commonly used to treat disorders such as arthritis, gastritis and osteoarthritis. The mechanism of cat's claw appears to be as an inhibitor of TNFα and antioxidant. Understanding the processes in osteoarthritis may facilitate and clarify the potential role of cat's claw as a complementary therapy to assist in the reduction of pro-inflammatory mediators and effectors. The clinical relevance of this therapy as a viable modality of intervention will be discussed.

Introduction

This paper seeks to explain the underlying mechanisms of cat's claw as a potential complementary therapy for the treatment of osteoarthritis. The pathophysiology of osteoarthritis and the mechanisms of cell injury and collagen degradation form the basis for discussing the therapeutic use of cat's claw. The properties of cat's claw are presented in relationship to the pathophysiology of osteoarthritis with a view to the use of Cats' Claw as an adjunct to treatment for this client group.

Osteoarthritis

Osteoarthritis is a common degenerative joint disease affecting at least 20 million adults in the United States. By the age of 40, approximately 90% of the people will have radiographic features in weight bearing joints indicating osteoarthritis[1] Degenerative joint disease is divided into two categories: primary and secondary. Primary affects some or all of the interphalangeal, metacarpophalangeal, and carpometatarsophalangeal joints, as well as the cervical and spine. Secondary may occur in any joint as a result acute or chronic articular injury.

Pathologically, articular cartilage is composed of collagen, water, proteoglycans, and chondrocytes. The cell matrix of the cartilage is regulated by chondrocytes which synthesizes the matrix, enzymatically digests it, and ultimately controls the matrix turnover. Destruction of the articular cartilage occurs through the release of catabolic enzymes, decreased production of inhibitors, and the ultimate breakdown of the matrix. During cell injury, as seen in the break down of the matrix, cytokines (catabolic mediators) are released.

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Cytokines such as Interleukin-1 (IL-1), tumor necrosis factor (TNFα), and nitric oxide (NO) are triggered by the chondrocytes, synoviocytes, fibroblasts and inflammatory cells.[2] Interleukin-1 is the catalyst for the production of destructive protease and inhibiting articular cartilage proteoglycan synthesis. Along with IL-1, two other interleukins, IL-17 and IL-18 have been found in osteoarthritis joints which also cause destructive proteases and induction of the synthesis of NO. NO is a gaseous mediator of cartilage pathology stimulated by IL-1, TNFα, and IL-17. NO has been implicated in the inhibition of proteoglycan synthesis and the progression of cartilage destruction.[3] TNFα is a driving force of IL-1 synthesis and regulation of cytokine production. Upregulation of the TNFα p55 receptor is associated with lost of articular cartilage.

Another mechanism associated with destruction of the cartilage is through NF-κB. IL-1 and TNFα allow the nuclear translocation of NF-κB which regulates genes involved in the inflammatory process.[4] NF-κB regulates the production of matrix metalloproteases (MMPs) by chondrocytes. During injury, chondrocytes release MMPs, which degrades the matrix.[5]

Joint injury is a complex event, involving acute cartilage injury generally resulting in cell death (necrosis, apoptosis, or both), release of cartilage proteoglycans, increased tissue water content and swelling, decreasing mechanical functionality, and increased sensitivity to cytokines. The pathophysiology of osteoarthritis is one of continuous injury and repair, resulting in failure to repair over time and cartilage destruction.

Mechanism of cell injury

Cartilage is made up of collagen fibers. Collagen fibers have chondrocytes that control the matrix turn over through the secretion of degradative enzymes such as MMPs and enrich the matrix with enzyme inhibitors. The rate of matrix break down is accelerated through mechanical injury resulting in the activation of catabolic enzymes and a decrease in the production of inhibitors. Chondrocytes react by increasing matrix production until a point is reached where repair cannot keep up with injury. Injury to the cell brings about leukocytes and macrophages which activate cytokines. Cytokines such as IL-1 which ''stimulates the chondrocytes to produce inducible nitric oxide synthase (iNOS) and TNF trigger the degradation process.''[2(p. 1304),6] TNF activates the transcription factor nuclear factor-κB (NF-κB) which has been associated with further inflammation. The activation of nuclear transcription factor κB has now been linked with a variety of inflammatory diseases.[7] Genes regulated by NF-κB include those involved in inflammatory responses and has been found to be a mediator of TNFα.[4]

Cat's claw

Cat's claw (Uña de Gato) Uña de Gais a herbal product sold as a phytomedicine in the United States. Uña de Gato, a vine from the basin of the Amazon River has been used in South America for numerous illnesses due to antioxidant and anti-inflammatory properties. In South America the bark of the vine is prepared as a decoction and drunk as a tea. Active chemicals in Cat's claw have been identified as quinovic acid glycosides,[8] sterols and oxidole.[9]

There are two species of cat's claw (*Uncaria tomentosa* and *Uncaria guianensis*) and both are used interchangeably in South America. However, differences between the species have been found with *U. tomentosa* which has a higher alkaloid content than *U. guianensis*. Commerical preparations of cat's claw (*U. tomentosa)* have been preferred because of the ease of standardization.[10]

Mechanism of cat's claw

Cat's claw has been found to inhibit lipopolysaccharide-induced iNOS gene expression, nitrate formation, cell death, PGE_2 production, the activation of NF-κB, and TNFα.[9–13] In addition, stimulations of IL-1 and 6 have been observed by cat's claw in rat models.[14]

Both species of cat's claw (*U. tomentosa* and *U. guianensis*), were found to suppress the redox-senitive regulation of gene expression, act as a free radical scavenger, suppress TNFα and apoptosis, and cytoprotective against potent oxidants such as peroxynitrite.[10] Specifically experiments to assess the ability of cat's claw to scavenge free radicals, 1,1-diphenyl-2-picrilhydrazl (DPPH), was performed. Free radicals are believed to cause tissue damage at the cellular level—harming DNA, mitochondria, and cell membranes. Free radicals can donate an electron to an appropriate acceptor (''reduction reaction'') or pair their unpaired electron by taking one from an appropriate donor (''oxidation reaction'') and have a major influence on the ''redox state'' in cells. Antioxidants are molecules which can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged. Cat's claw has been

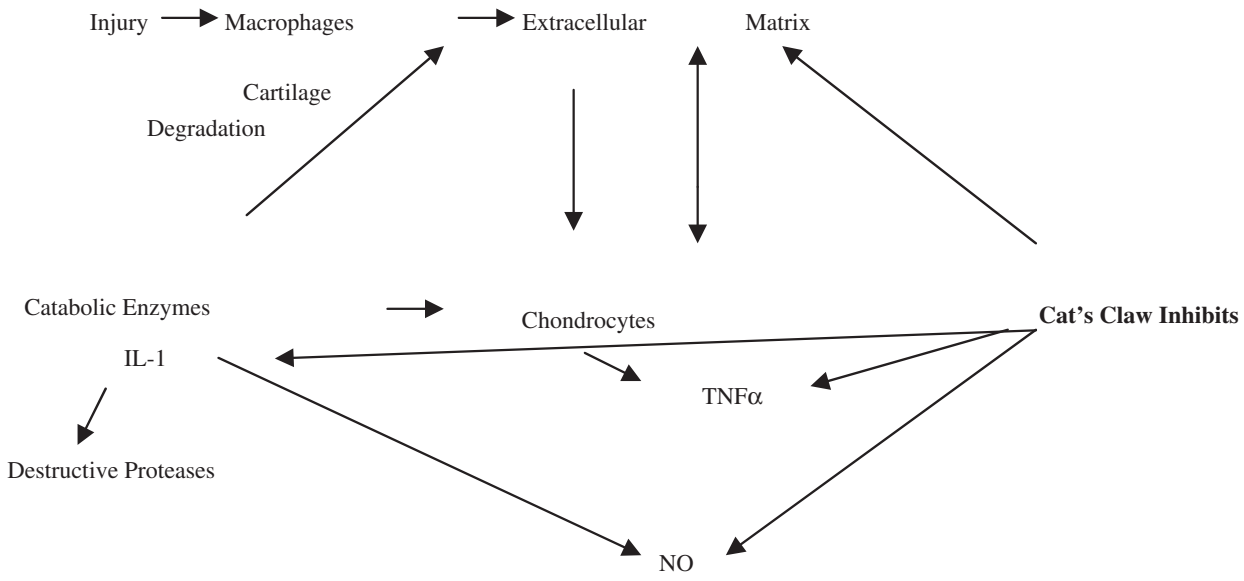

Figure 1 Mechanism of cat's claw on extracellular matrix in osteoarthritis.

shown to be an antioxidant, that can influence cell death through scavenging DPPH.[9]

The suppression of TNFα was noted to be at levels far less than that required for antioxidants[13] which results in cat's claw's ability to inhibit the activation of NK-κB. The transcription factor NK-κB is a redox-sensitive transcription that regulates the expression of genes involved in osteoarthritis.[15]

The role of cat's claw as an inhibitor of NF-κB is important in the treatment of osteoarthritis since two widely used anti-inflammatory agents, salicylates and glucorticoids are both inhibitors of NF-κB.[4]

Model explicating treatment

In order to understand the how cat's claw influences the pathophysiology of osteoarthritis, Fig. 1 is a diagram displaying cell injury and the points at which cat's claw impacts the disease. This figure is based upon an understanding of cell injury, which causes macrophages and lymphocytes to be activated with persistent cellular damage of the extracellular matrix. This continuous damage results in decreased metalloproteinase activity, and increased cytokine production. Several points in this trajectory have been identified as where cat's claw can intervene to decrease collagen degradation.

Complementary therapies

As practitioners, we are obligated to ask clients about their use of complementary therapies as well be knowledgeable in answering patient questions. While cat's claw is widely recognized as an appropriate intervention in South American, for chronic inflammation, and pain, our understanding of the mechanism underlying its success is still being examined. As patients search for answers for symptom control, more individuals will gain information on complementary treatments such as cat's claw. Therefore, practitioners must continue to learn about complementary therapies and the basis for their utilization.

Summary

Cat's claw is a herbal medicine that is being used to treat inflammatory disorders, osteoarthritis, and gastritis. Numerous research studies have been conducted supporting cat's claw as a viable pharmaceutical in the treatment of osteoarthritis.[13] The pathology of osteoarthritis, specifically the decrease in the degradation of collagen through inhibition of cytokines and antioxidant properties allow cat's claw to be effective.

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