

What's All This in My Dog's Arthritis Supplement?

Yucca, feverfew, bromelain, devil's claw, cat's claw, and avocado – botanical potpourris like these, created specifically for animals with arthritis, are blossoming like dandelions in pet stores and catalogs. And, like dandelions, these pills, powders, and poultices packed with phytopharmaceuticals may possess surprisingly effective medicinal merit. They are undoubtedly attracting customers. Herbal arthritis formulae give consumers hope of lessening their animals' suffering without the worry of liver damage and gastrointestinal ulceration. Some manufacturers claim that their products will even reverse degenerative changes like glucosamine and chondroitin.

Are they effective? They probably are, to a degree. A 2006 Cochrane review of herbal medicine for humans with low back pain concluded, "Although there are good results with three herbal medicines [devil's claw, white willow bark, and topical cayenne] in short-term trials, with strong evidence for a particular form of one of the herbal medicines, there is no evidence yet that any of these substances are safe and useful for long term use."¹ Extrapolating human studies to animal applications demands caution due to physiologic differences between species. Consider, for example, the concern about aspirin-like compounds in white willow bark. This limits its application in feline patients. Other species- or breed-specific metabolic idiosyncrasies may arise with further study. Fortunately, though, more veterinary studies are becoming available, such as one in 2004, showing value for boswellia extract for canine inflammatory joint and spinal disease.²

The herb "devil's claw" (*Harpagophytum procumbens*) has become particularly popular in holistic circles. *In vitro* studies suggest that devil's claw offers analgesic, anti-inflammatory, and anti-oxidant effects.³ Results from two randomized, controlled trials in humans suggest that devil's claw delivered a statistically significant benefit in pain control over placebo.⁴



Freeze-dried cat's claw (*Uncaria guianensis*), from an Amazonian medicinal plant, provided strong and safe analgesia in patients with osteoarthritis of the knee in a placebo-controlled, double blind, human trial.⁵

¹ Gagnier JJ, vanTulder M, Berman B, and Bombardier C. Herbal medicine for low back pain. *The Cochrane Database of Systematic Reviews*. 2006, Issue 2. Art No.:CD004504.pub3. DOI: 10.1002/14651858.CD004504.pub3.

² Reichling J, Schmokel H, Fitz J, Bucher S, Saller R. Dietary support with Boswellia resin in canine inflammatory joint and spinal disease. *Scweiz Arch Tierheilkd*. 2004;146(2):71-79.

³ Studies cited in: Walker-Bone K. 'Natural remedies' in the treatment of osteoarthritis. *Drugs Aging*. 2003;20(7):517-526.

⁴ Studies cited in: Walker-Bone K. 'Natural remedies' in the treatment of osteoarthritis. *Drugs Aging*. 2003;20(7):517-526.

How do these herbs work? Understanding the mechanisms of action of phytopharmaceuticals on chondrocyte anabolism and catabolism is important, in that it allows one to tailor the herbal approach to the patient's specific disease process. Cytokines, both pro- and anti-inflammatory, are also important components to consider when managing arthritis pain. For example, the cytokine TNF- α appears to be involved in the pathogenesis and progression of osteoarthritis; cat's claw reduces TNF- α synthesis.^{6 7} Cat's claw likewise inhibits TNF- α gene expression within the gastric mucosa in cases of gastritis secondary to NSAID usage.⁸



Avocado products are increasingly prominent in companion animal foods. Avocado/Soybean Unsaponifiables (ASU's), derived from unsaponifiable fractions of avocado and soybean oils, may deliver structure-modifying activity.⁹ One placebo-controlled trial in humans demonstrated that ASU's significantly reduced joint space narrowing compared to placebo for a subgroup of patients with the most dramatic joint space reduction.¹⁰ ASU's may affect joint surfaces by increasing production of TGF- β 1, decreasing matrix metalloproteinase production, and promoting chondrocyte synthesis of matrix components.¹¹

In contrast to the increase in joint levels of TGF- β 1 from ASU administration, the oral proteolytic enzymes, bromelain and papain, appear to reduce blood TGF- β levels in some disease states.¹² These include diseases characterized by overproduction of TGF- β 1, such as rheumatoid arthritis and radiation-induced

⁵ Piscoya J, Rodriguez Z, Bustamante SA, 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 Res.* 2001;50:442-448.

⁶ Malemud CJ. Cytokines as therapeutic targets for osteoarthritis. *Biodrugs.* 2004;18(1):23-35.

⁷ Sandoval M, Okuhama NN, Zhang X-J, Condezo LA, et al. Anti-inflammatory and antioxidant activities of cat's claw (*Uncaria tomentosa* and *Uncaria guianensis*) are independent of their alkaloid content. *Phytomedicine.* 2002;9:325-327.

⁸ Miller MJS, Zhang XJ, Charbonnet RM, Clark DA, et al. The anti-inflammatory actions of the herbal medicine, cat's claw, are due to a suppression of NF-kappabeta activation and inhibition of gene expression. *Pediatric Res.* 1999;45:114A (abstract). Cited in: Piscoya J, Rodriguez Z, Bustamante SA, et al. Efficacy and safety o-f freeze-dried cat's claw in osteoarthritis of the knee: mechanisms of action of the species *Uncaria guianensis*. *Inflammation Res.* 2001;50:442-448.

⁹ Walker-Bone K. 'Natural remedies' in the treatment of osteoarthritis. *Drugs Aging.* 2003;20(7):517-526.

¹⁰ Lequesne M, Maheu E, Cadet C, et al. Structural effect of avocado/soybean unsaponifiables on joint space loss in osteoarthritis of the hip. *Arthritis Rheum.* 2002; 47:50-58. Cited in: Walker-Bone K. 'Natural remedies' in the treatment of osteoarthritis. *Drugs Aging.* 2003;20(7):517-526.

¹¹ Henrotin Y, Sanchez C, and Balligand M. Pharmaceutical and nutraceutical management of canine osteoarthritis: Present and future perspectives. *The Veterinary Journal.* 2005;170:113-123.

¹² Desser L, Holomanova D, Zavadova E, et al. Oral therapy with proteolytic enzymes decreases excessive TGF- β levels in human blood. *Cancer Chemothera. Pharmacol.* 2001;47(Suppl):S10-S15.

fibrosis. In clinical trials, an oral enzyme preparation consisting of bromelain, trypsin, and a rutin derivative provided improvements in arthritis patients comparable to diclofenac, with fewer adverse effects.^{13 14}

Lastly, several anti-arthritis botanical products possess anti-oxidant activity, which help reduce tissue damage associated with inflammation. Some products, like yucca, supply a wide variety of benefits, including anti-oxidant, anti-inflammatory, and even anti-protozoal effects. Yucca has earned increased recognition among animal feed producers for many reasons, in addition to anti-arthritis applications. For more information on yucca, see below.



A closer look at yucca (*Yucca schidigera*)

Yucca, a member of the lily family, is native to deserts in the southwest US and northern Mexico, and appears frequently as an ingredient in animal arthritis supplements. Yucca contains a diverse array of physiologically active phytochemicals useful for arthritis. Additionally, many consumers have likely caught wind of yucca's capacity to reduce malodorous fecal odors and flatulence in dogs.^{15 16}

¹³ Akhtar NM, Naseer R, Farooqi AZ, et al. Oral enzyme combination versus diclofenac in the treatment of osteoarthritis of the knee – a double-blind prospective randomized study. *Clin Rheumatol.* 2004;23:410-415.

¹⁴ Klein G, Kullich W, Schnitker J, et al. Efficacy and tolerance of an oral enzyme combination in painful osteoarthritis of the hip. A double-blind, randomized study comparing oral enzymes with non-steroidal anti-inflammatory drugs. *Clinical and Experimental Rheumatology.* 2006;24:25-30.

¹⁵ Lowe JA, Kershaw SJ, Taylor AJ, et al. The effect of *Yucca schidigera* extract on canine and feline faecal volatiles occurring concurrently with faecal aroma amelioration. *Res Vet Sci.* 1997;63(1):67-71.

¹⁶ Giffard CJ, Collins SB, Stoodley NC, Butterwick RF, et al. Administration of charcoal, *Yucca schidigera*, and zinc acetate to reduce malodorous flatulence in dogs. *JAVMA.* 2001;218(6):892-896.

Yucca provides a rich supply of steroidal saponins. Saponins consist of a lipophilic nucleus and one or more side chains of hydrophilic carbohydrates.¹⁷ The dual fat- and water-soluble characteristics of yucca saponins allow them to form complexes with cholesterol and protozoal membranes. A relationship between anti-protozoal and anti-arthritis mechanisms has been proposed by some authors.¹⁸

Another important class of chemicals found in yucca includes polyphenolic compounds, such as resveratrol. Polyphenols help reduce inflammation by inhibiting the nuclear transcription factor NFkappaB. (NFkB is responsible for promoting the formation of nitric oxide (NO) by increasing production of inducible nitric oxide synthase (iNOS). NO is an agent of inflammation, and tissue levels of NO increase during inflammatory states.) Yucca polyphenols have potent anti-oxidant and free-radical scavenging activity. They exhibit anti-aggregation activity against platelets, and platelet aggregation is one of many characterizing features of inflammation.

¹⁷ Cheeke PR, Piacente S, and Oleszek W. Anti-inflammatory and anti-arthritis effects of yucca schidigera: a review. *Journal of Inflammation*. 2006;3:6

¹⁸ Cheeke PR, Piacente S, and Oleszek W. Anti-inflammatory and anti-arthritis effects of yucca schidigera: a review. *Journal of Inflammation*. 2006;3:6