

## RESEARCH NEWS

An equine nutraceutical 'Hyalcare' is featured in a research paper recently accepted for publication in the Journal of Veterinary Pharmacology and Therapeutics. The research, conducted at the University of Guelph, by Cantox Scientist-Wendy Pearson, is the fourth research project funded by Selected Bioproducts Ltd (Guelph Ontario) as part of their "Herbs for Horses" product development program. Hyalcare was shown to inhibit nitric oxide and protect cartilage from breakdown in a cell culture model of arthritis. Researchers concluded that Hyalcare may be a useful adjunct for treatment of arthritis and protection of cartilage. Selected Bioproducts have also published research results for three other products: 'Breathe' significantly reduced respiratory rate in horses with COPD (Canadian Journal of Veterinary Research 2007; 71(2):145-51), and 'Mobility' reduced cartilage damage in a cell culture model of arthritis (Journal of Veterinary Pharmacology and Therapeutics 2007; 30(6):523-33) and reduced PGE<sub>2</sub> in synovial fluid of horses with naturally occurring arthritis (Journal of Nutraceuticals, Functional and Medical Foods 1999; 2(2):31-46).

### Do you have some exciting research data on one of your products?

Find out how you can highlight it in our newsletter by sending an email to [agri@cantox.com](mailto:agri@cantox.com).

## HOT OFF THE PRESS...

- Pearson W, Orth MW, Karrow NA, MacLusky N, Lindinger MI. 2007 Anti-inflammatory and chondroprotective effects of nutraceuticals in a cartilage explant model of inflammation. *Molecular Nutrition and Food Research*: 51(8):1020-30.
- Pearson W, Omar S, McKee S, Clarke AF. 2007 Low-dose ginseng (*Panax quinquefolium*) modulates timecourse and magnitude of antibody response to equine herpesvirus (EHV-1) vaccination in horses. *Canadian Journal of Veterinary Research*: 71(3):213-7
- Pearson W, Charch A, Brewer D, Clarke AF. 2007 Supplementation with an herbal composite alleviates clinical signs of respiratory dysfunction in horses with recurrent airway obstruction (RAO). *Canadian Journal of Veterinary Research*, 71(2):145-51.

## Upcoming Events

Come and visit Cantox representatives at the following conferences:

- Mar 25-26, 2008  
Mid-Atlantic Veterinary Nutrition Conference  
(Baltimore, MD)  
<http://manc.umd.edu/>
- Apr 18-19, 2008  
European Equine Health and Nutrition Congress (Wageningen, Netherlands)  
<http://www.equine-congress.com/>
- Aug 3-8, 2008  
Society for Medicinal Plant Research Annual Meeting (Athens, Greece)  
<http://www.ga-online.org/files/Athens/FA2008.pdf>
- Sep 10-13, 2008  
British Equine Veterinary Association Congress  
(Liverpool, UK)  
<http://www.beva.org.uk/node/299>
- Nov 9-14, 2008  
4th World Congress on Medicinal and Aromatic Plants  
(Cape Town, South Africa)  
<http://web.up.ac.za/default.asp?ipkCategoryID=4943&ArticleID=15>
- Dec 6-10, 2008  
54th Annual Meeting of the American Association of Equine Practitioners (San Diego CA)  
<http://www.aaep.org/convention.htm>

Welcome to the first edition of ANIMAL NUTRA. This quarterly newsletter produced by Cantox Health Sciences International will keep you up-to-date on new research results, brief reviews of current research, and exciting events of interest to the global market for veterinary nutraceuticals. Email us with your research news, upcoming events and business news items at [agri@cantox.com](mailto:agri@cantox.com). This newsletter is provided for informational purposes only and does not represent endorsement by Cantox for any products mentioned.

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HEALTH SCIENCES INTERNATIONAL

# Mini Review

## Devil's Claw (*Harpagophytum procumbens*)

Chronic arthritis is one of the most common conditions for which nutraceuticals and complementary therapies are used in horses and companion animals. This is due in part to the fact that those drugs we typically use to manage pain associated with arthritis [i.e., Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)] have well-known adverse effects, including gastric ulceration<sup>1</sup> and inhibition of cartilage re-synthesis<sup>2</sup> without reducing inflammation-associated cartilage breakdown.<sup>3,4</sup> For these reasons, alternatives to allopathic medications are often sought for arthritic conditions in animals.

Devils Claw (*Harpagophytum procumbens*) has been the subject of vigorous scientific study and commercial acclaim. Its bioactivity appears to be concentrated in the roots, and is thought to result primarily from iridoids (especially harpagoside<sup>5</sup>) with some possible contribution by flavonoids.<sup>6</sup> *H. procumbens* is a popular ingredient in anti-inflammatory supplements for horses, dogs, cats and camelids and has been well-investigated by the scientific community for anti-inflammatory activity. While no anti-inflammatory research on *H. procumbens* alone has been reported in important veterinary species, there are isolated reports of vet-directed products containing *H. procumbens* showing benefits in a cartilage model of arthritis<sup>3</sup> and in horses with naturally-occurring arthritis.<sup>7</sup> An extended

abstract describing an inhibitory effect of *H. procumbens* on blood pressure and cardiac contractility in anaesthetized dogs suggests an effect of the plant on vascular function but the veterinary implications of this study are unclear.<sup>6</sup>

Recent reviews of clinical research in humans have attributed moderate anti-inflammatory activity to *H. procumbens* products delivering >50 mg harpagoside/day (0.7 mg/kg bw) in patients with osteoarthritis and/or low back pain.<sup>8,9</sup> A single oral dose *H. procumbens* extract (>19 mg harpagoside/kg bw) significantly reduced pain responses in formalin-challenged mice,<sup>10</sup> and lyophilized crude aqueous extract of *H. procumbens* reduced pain associated with acetic acid and heat in mice (>50 mg/kg bw i.p.; harpagoside content was not determined).<sup>11</sup> There is a growing body of *in vitro* research which points to Cox-2 inhibitory action of devil's claw<sup>12-14</sup> which may contribute to the analgesic effect of the plant. *H. procumbens* is without significant adverse events at bioactive doses in humans<sup>15</sup> and rodents.<sup>12</sup> Aqueous extract of the plant has an LD<sub>50</sub> of 1250 ± 156 mg/kg in mice.<sup>12</sup>



1. Monreal et al. Lower gastric ulcerogenic effect of suxibuzone compared to phenylbutazone when administered orally to horses. *Res Vet Sci.* 2004 Apr;76(2):145-9.
2. Beluche et al. Effects of oral administration of phenylbutazone to horses on *in vitro* articular cartilage metabolism. *Am J Vet Res.* 2001 Dec;62(12):1916-21.
3. Pearson et al. Differential anti-inflammatory and chondroprotective effects of simulated digests of indomethacin and an herbal composite (Mobility) in a cartilage explant model of articular inflammation. *J Vet Pharmacol Ther.* 2007 Dec;30(6):523-33.
4. Jeffrey and Aspden. Cyclooxygenase inhibition lowers prostaglandin E2 release from articular cartilage and reduces apoptosis but not proteoglycan degradation following an impact load *in vitro*. *Arthritis Res Ther.* 2007;9(6):R129.
5. Qi et al. Iridoid glycosides from *Harpagophytum procumbens* D.C. (devil's claw). *Phytochemistry.* 2006 Jul;67(13):1372-7.
6. Occhiuto and De Pasquale. Electrophysiological and haemodynamic effects of some active principles of *Harpagophytum procumbens* DC in the dog. *Pharmacol Res.* 1990 Sep-Oct;22 Suppl 3:72-3.
7. Pearson et al. Effect of a proprietary herbal product on equine joint disease. *JNFMF.* 1999;2(2):31-46.
8. Denner. A review of the efficacy and safety of devil's claw for pain associated with degenerative musculoskeletal diseases, rheumatoid, and osteoarthritis. *Holist Nurs Pract.* 2007 Jul-Aug;21(4):203-7.
9. Gagnier et al. *Harpagophytum procumbens* for osteoarthritis and low back pain: a systematic review. *BMC Complement Altern Med.* 2004 Sep 15;4:13.
10. Uchida et al. Antinociceptive effects of St. John's wort, *Harpagophytum procumbens* extract and Grape seed proanthocyanidins extract in mice. *Biol Pharm Bull.* 2008 Feb;31(2):240-5.
11. Mahomed et al. Analgesic, anti-inflammatory and antidiabetic properties of *Harpagophytum procumbens* DC (Pedaliaceae) secondary root aqueous extract. *Phytother Res.* 2004 Dec;18(12):982-9.
12. Huang et al. Harpagoside suppresses lipopolysaccharide-induced iNOS and COX-2 expression through inhibition of NF-kappa B activation. *J Ethnopharmacol.* 2006 Mar 8;104(1-2):149-55.
13. Kundu et al. Inhibitory effects of the extracts of *Sutherlandia frutescens* (L.) R. Br. and *Harpagophytum procumbens* DC. on phorbol ester-induced COX-2 expression in mouse skin: AP-1 and CREB as potential upstream targets. *Cancer Lett.* 2005 Jan 31;218(1):21-31.
14. Na et al. Inhibition of phorbol ester-induced COX-2 expression by some edible African plants. *Biofactors.* 2004;21(1-4):149-53.
15. Vlachojannis et al. Systematic review on the safety of *Harpagophytum* preparations for osteoarthritic and Low back pain. *Phytother Res.* 2008 Feb;22(2):149-52.

## Regulatory News

### North America

**Aug 2007** – Health Canada proposes a new definition for Veterinary Natural Health Products

**Dec 2007** – Center for Veterinary Medicine in the US issued its final regulations on the index of legally Marketed Unapproved New Animal Drugs for Minor Species (MUMS) <http://www.fda.gov/cvm/minortoc.htm>

### Global

**Jan 2008** – Closer ties are being created between European and Canadian regulatory authorities in regards to both Human and Animal medicines – Confidentiality agreements will allow the exchange of information between countries both before and after a medication has been approved.

**Jan 2008** – Australian Pesticides and Veterinary Medicines Authority appointed new CEO Dr. Eva Bennet-Jenkins

## In Profile with...

### Cantox Health Sciences International

Cantox has been helping clients resolve complex scientific and toxicology issues, plan scientific and regulatory strategies and compliance plans while facilitating timely regulatory approvals globally for over 20 years. In order to help future clients with up and coming developments in veterinary nutraceuticals and natural health products, Cantox has hired an expert in this field, Wendy Pearson, PhD. Wendy, a research expert with knowledge of the development and analysis of veterinary nutraceuticals will lead Cantox's strong team of toxicologists and regulatory experts to exceed any client's needs.

A significant goal is to help industry leaders by informing and educating them on the latest regulations and news in this field. Our newsletter is one of the means by which we'll achieve this goal; we're also offering our readers the opportunity to profile their company and what's new in our "In Profile" section. If you would like to profile your company please contact Cantox at [agri@cantox.com](mailto:agri@cantox.com). Let others know of new products, research or hurdles you have overcome.

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