Literature Cited

1. Lippiello L, Walsh T, Fienhold M. The association of lipid abnormalities with tissue pathology in human osteoarthritic articular cartilage. Metabolism 1991;40:571-576.
2. Curtis CL, Hughes CE, Flannery CR, et al. n-3 fatty acids specifically modulate catabolic factors involved in articular cartilage degradation. J Biol Chem 2000;275:721 - 724.
3. Munsterman A, Bertone A, Zachos T, et al. Effects of the omega-3 fatty acid, alpha-linolenic acid, on lipopolysaccharide-challenged synovial explants from horses. Am J Vet Res 2005;66:1503-1508.
4. Maroon JC, Bost JW. [omega]-3 Fatty acids (fish oil) as an anti-inflammatory: an alternative to nonsteroidal anti-inflammatory drugs for discogenic pain. Surgical Neurology 2006;65:326-331.
5. Diehl H, May E. Cetyl Myristoleate Isolated from Swiss Albino Mice: An Apparent Protective Agent against Adjuvant Arthritis in Rats. J Pharmac Sci 1994;83:296-299.
6. Hunter KW, Gault RA, Stehouwer JS, et al. Synthesis of cetyl myristoleate and evaluation of its therapeutic efficacy in a murine model of collagen-induced arthritis. Pharmacological Research 2003;47:43-47.
7. Hesslink RJ, Armstrong DI, Nagendran M, et al. Cetylated fatty acids improve knee function in patients with osteoarthritis. J Rheumatol 2002;29:1708-1712.
8. Piperno M, Reboul P, Hellio Le Graverand MP, et al. Glucosamine sulfate modulates dysregulated activities of human osteoarthritic chondrocytes in vitro. Osteoarthritis and Cartilage 2000;8:207-212.
9. Dodge GR, Jimenez SA. Glucosamine sulfate modulates the levels of aggrecan and matrix metalloproteinase-3 synthesized by cultured human osteoarthritis articular chondrocytes. Osteoarthritis and Cartilage 2003;11:424-432.
10. Reginster JY, Deroisy R, Rovati LC, et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. The Lancet 2001;357:251-256.
11. Muller-Fabender H, Bach GL, Haase W, et al. Glucosamine sulfate compared to ibuprofen in osteoarthritis of the knee. Osteoarthritis and Cartilage 1994;2:61-69.
12. Wang Y, Prentice L, Vitetta L, et al. The effect of nutritional supplements on osteoarthritis. Altern Med Rev 2004;9:275-296.
13. Tiraloche G, Girard C, Chouinard L, et al. Effect of oral glucosamine on cartilage degradation in rabbit model of osteoarthritis. Arthritis Rheum 2005;52:1118 - 1128.
14. Fenton J, Chlebek-Brown K, Caron J, et al. Effect of glucosamine on interleukin-1-conditioned articular cartilage. Equine Vet J 2002:219-223.
15. Fenton JI, Chlebek-Brown KA, Peters TL, et al. Glucosamine HCl reduces equine articular cartilage degradation in explant culture. Osteoarthritis and Cartilage 2000;8:258-265.
16. Kim LS, Axelrod LJ, Howard P, et al. Efficacy of methylsulfonylmethane (MSM) in osteoarthritis pain of the knee: a pilot clinical trial. Osteoarthritis and Cartilage 2006;14:286-294.
17. Usha P, Naidu M. Randomised, double-blind, parallel, placebo-controlled study of oral glucosamine, methylsulfonylmethane and their combination in osteoarthritis. Clin Drug Invest 2004;24:353-363.
18. Rizzo R, Grandolfo M, Godeas C, et al. Calcium, sulfur, and zinc distribution in normal and arthritic articular equine cartilage: a synchrotron radiation-induced X-ray emission (SRIXE) study. J Exp Zool 1995;273:82-86.
19. DiSilvestro RA, DiSilvestro DJ, DiSilvestro DJ. Methylsulfonylmethane (MSM) Intake in Mice Produces Elevated Liver Glutathione and Partially Protects Against Carbon Tetrachloride-Induced Liver Injury. FASEB J 2008;22:445.448-.
20. Hegewald A, Ringe J, Bartel J, et al. Hyaluronic acid and autologous synovial fluid induce chondrogenic differentiation of equine mesenchymal stem cells: a preliminary study. Tissue Cell 2004;36:431-438.
21. Kawcak C, Frisbie D, Trotter G, et al. Effects of intravenous administration of sodium hyaluronate on carpal joints in exercising horses after arthroscopic surgery and osteochondral fragmentation. Am J Vet Res 1997;58:1132-1140.
22. Schauss AG, Balogh L, Polyak A, et al. Absorption, distribution and excretion of 99mtechnetium labeled hyaluronan after single oral doses in rats and beagle dogs. FASEB Journal 2004;18:Abst. 129.124.
23. Bergin B, Pierce S, Bramlage L, et al. Oral hyaluronan gel reduces post operative tarsocrural effusion in the yearling Thoroughbred. Equine Vet J 2006;38:375-378.
24. Henrotin YE, Labasse AH, Jaspar JM, et al. Effects of three avocado/soybean unsaponifiable mixtures on metalloproteinases, cytokines and prostaglandin E2 production by human articular chondrocytes. Clin Rheumatol 1998;17:31 - 39.
25. Henrotin Y, Sanchez C, Deberg M, et al. Avocado/soybean unsaponifiables increase aggrecan synthesis and reduce catabolic and proinflammatory mediator production by human osteoarthritic chondrocytes. J Rheumatol 2003;30:1825-1834.
26. 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.
27. Kawcak CE, Frisbie DD, McIlwraith CW, et al. Evaluation of avocado and soybean unsaponifiable extracts for treatment of horses with experimentally induced osteoarthritis. American Journal of Veterinary Research 2007;68:598-604.
28. McAlindon TE, Jacques P, Zhang Y, et al. Do antioxidant micronutrients protect against the development and progression of knee osteoarthritis? Arthritis Rheum 1996;39:648 - 656.
29. Blankenhorn G. Clinical effectiveness of Spondyvit (vitamin E) in activated arthroses. A multicenter placebo-controlled double-blind study [Abstract only. Article in German]. Z Orthop Ihre Grenzgeb 1986;124:340-343.
30. Edmonds SE, Winyard PG, Guo R, et al. Putative analgesic activity of repeated oral doses of vitamin E in the treatment of rheumatoid arthritis. Results of a prospective placebo controlled double blind trial. Ann Rheum Dis 1997;56:649-655.
31. Kurz B, Jost B, Schunke M. Dietary vitamins and selenium diminish the development of mechanically induced osteoarthritis and increase the expression of antioxidative enzymes in the knee joint of STR/1N mice. Osteoarthritis and Cartilage 2002;10:119-126.
32. Carlisle E. In vivo requirement for silicon in articular cartilage and connective tissue formation in the chick. J Nutr 1976;106:478-484.

EDUCATIONAL PARTNER AAEP PLATINUM PERFORMANCE®

Where good nutrition meets good medicine™

1-866-553-2400 www.platinumvet.com

(Mon-Thurs 6am- 5:30pm PST, Fri 6am- 5pm PST)

P.O. Box 990, Buellton, CA 93427

Supplementing for Joint Health

Tara Hembrooke, PhD, MS

Although joint disease develops for a variety of reasons in horses, a common cause is persistent inflammation. Under such conditions, uncontrolled free radical activity and dysregulation of local enzymes degrade critical components of cartilage, synovial fluid and the synovial membrane. The joint pain that arises as a result of these processes is a significant cause of lameness and "loss of use." To combat these problems, Platinum Performance™ has released Platinum Performance™ CJ, a comprehensive joint care formula that includes omega-3 fatty acids, glucosamine, methylsulfonylmethane, hyaluronic acid, avocado/soy unsaponifiables, cetyl-myristoleate, antioxidants and minerals. The effects of each of these components of Platinum Performance™ CJ will be discussed.

Fatty Acids

Omega-3 fatty acids and their metabolites generally have anti-inflammatory effects, which is in contrast to the pro-inflammatory effects of the metabolites of omega-6 fatty acids. In fact, the severity of articular cartilage lesions can be linked to the amount of omega-6 fatty acids in the cartilage.[1] Omega-3 fatty acids, on the other hand, have a protective role. For example, joint components treated with α-linolenic acid, an omega-3 fatty acid, produce less pro-inflammatory mediators such as interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF-α), and prostaglandin E_2 (PGE_2).[2,3] Furthermore, the analgesic effects of omega-3 fatty acids suggest that they may be a safe alternative to non-steroidal anti-inflammatory drugs.[4]

Cetyl-myristoleate, an ester of an omega-5 fatty acid, has also demonstrated effectiveness in improving arthritic pain and mobility. Initial studies indicated injected cetyl-myristoleate blocks inflammation and protects rats and mice against experimentally-induced arthritis.[5,6] More recently, human dietary supplementation has significantly improved knee range of motion and functionality.[7]

Glucosamine

Glucosamine, an amino sugar, is a precursor to the compression-resistant components of cartilage called glycosaminoglycans, or GAGS. Glucosamine decreases the activities of collagen-degrading enzymes and increases cartilage protein synthesis.[8,9] Long-term supplementation studies in humans indicate that glucosamine slows the progression of osteoarthritis[10] and may also be as efficacious as ibuprofen in relieving

EDUCATIONAL PARTNER AAEP PLATINUM PERFORMANCE®

Where good nutrition meets good medicine™

1-866-553-2400 www.platinumvet.com

arthritic pain.[11] The results of similar studies in animals indicate that glucosamine supplementation reduces the ill effects of osteoarthritis on cartilage and subchondral bone,[12,13] and treatment of equine cartilage explants with glucosamine reduces the destructive effects of interleukin 1-ß and synthesis of inflammatory mediators.[14,15]

Methylsulfonylmethane

Due to its analgesic and anti-inflammatory effects, methylsulfonylmethane (MSM), a sulfur-containing metabolite of dimethyl sulfoxide, is often advocated for joint pain. In human studies, dietary supplementation with MSM has successfully reduced joint pain, either alone or when consumed in combination with glucosamine.[16,17] Because the sulfur content of arthritic cartilage is approximately one-third that of healthy cartilage,[18] MSM often is advocated as a source of sulfur. Antioxidant properties of MSM have also recently been documented.[19]

Hyaluronic Acid

Hyaluronic acid is a key component of synovial fluid that nourishes, lubricates, and protects the joint. It is part of the building blocks for proteoglycans, such as aggrecan, stimulates the formation of cartilage components from equine stem cells,[20] and has anti-inflammatory actions in the synovial fluid by inhibiting PGE_2.[21] Although hyaluronic acid commonly is administered intra-articularly, orally administered hyaluronic acid has been shown to be bio-available[22] and effective in reducing post-operative joint inflammation in horses.[23]

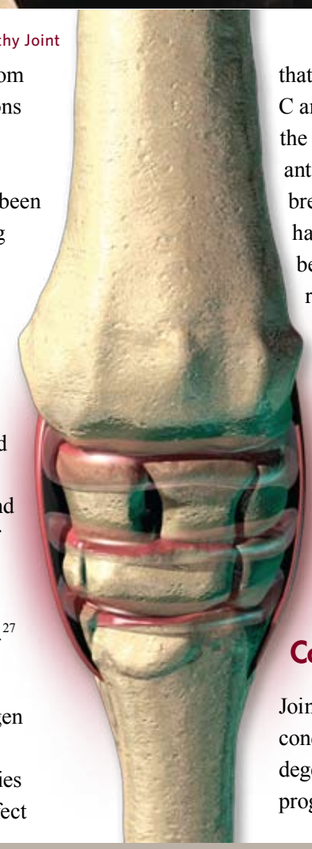
Avocado/Soy Unsaponifiables

Avocado/Soy unsaponifiables (ASU) are comprised of oil fractions from avocado and soy. The results of *in vitro* studies with ASU demonstrate its ability to increase aggrecan synthesis, prevent IL-1-induced decreases in aggrecan production, and reduce expression or production of degradative enzymes and inflammatory proteins.[24,25] ASU supplementation of humans with osteoarthritis reduces the loss of joint space,[26] and horses consuming ASU have increased GAG synthesis and reduced breakdown of cartilage.[27]

Micronutrients

Recently, oxidative damage caused by reactive oxygen species has been implicated in the development of joint disorders in horses. These radical oxygen species promote the degradation of joint components, an effect

Unhealthy Joint



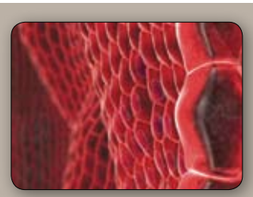
that can be counteracted by antioxidants such as vitamins C and E. For example, not only is vitamin C crucial for the development of cartilage, but its well-documented antioxidant effects may also protect against cartilage breakdown.[28] The fat-soluble antioxidant, vitamin E, has demonstrated analgesic and mobility-enhancing benefits in individuals with arthritis[29,30] and has been reported to protect against joint disorders in mice prone to osteoarthritis.[31] Of the other micronutrients in Platinum Performance™ CJ, silicon is important because it is required for normal formation of cartilage and bones. In fact, consumption of diets deficient in silicon by growing chicks results in abnormalities in articular cartilage formation, bone development, and growth of the comb[32] – a structure that is abundant in connective tissue and hyaluronic acid.

Conclusion

Joint disorders in horses are serious and debilitating conditions. The multiple possible causes of joint degeneration require a comprehensive nutritional program that addresses each contributing factor. Provision of omega-3 fatty acids, glucosamine, methylsulfonylmethane, hyaluronic acid, avocado/soy unsaponifiables, cetyl-myristoleate, antioxidants, and silicon modulates one or more of the major factors associated with joint disorders. Platinum Performance™ offers solutions for complete joint health with the new Platinum Performance™ CJ, Platinum Performance™ Equine, Ortho-Chon™ or Ortho-Chon™ HA.

Putting it into Practice

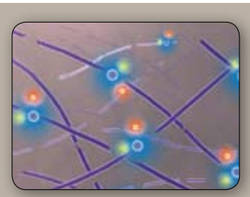
- Reduce feeds with an imbalance of omega-3 and omega-6 fatty acids such as grains, corn oil and some commercial feeds.
- Encourage consumption of omega-3 fatty acids and antioxidants by increasing the horse's intake of forage and pasture grazing.
- Supplement with Platinum Performance™ Equine on a daily basis to protect the joint from inflammation and oxidative stress.
- For horses with existing joint problems or those prone to developing joint problems, supplement with Platinum Performance™ CJ.



Inflammation

Chronic Inflammation

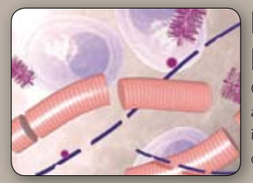
Omega-3 fatty acids, Glucosamine, Avocado/Soybean Unsaponifiables, Cetyl-Myristoleate, Antioxidants such as Vitamin C and Vitamin E, and botanical compounds such as Boswellia, decrease inflammatory responses.



Free Radical Damage

Free Radical Damage

Antioxidants and supplemental hyaluronic acid help protect the joint against degeneration caused by free radical damage and help maintain synovial fluid viscosity and normal joint function.



Enzymatic Activity

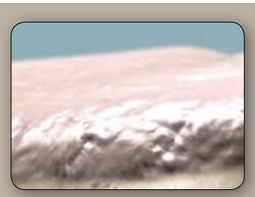
Degradative Enzyme Activity

Omega-3 fatty acids decrease the activity of aggrecanase enzymes in the joint and, therefore, reduce cartilage degradation.

Traumatic Injury or Overuse

Traumatic Injury or Overuse

Omega-3 fatty acids, antioxidants, silicon, MSM and ASU help slow degeneration and stimulate repair of cartilage. Silicon also supports bone density, cartilage synthesis and tendon and ligament strength.



Low-Grade Cartilage Damage

Natural Aging Process

Omega-3 fatty acids, antioxidants, and cartilage building nutrients protect against degeneration, which naturally occurs with age.

5 Major Contributors to Joint Disease