KAM = 0.12 and 0.05%Nnm/BW-HT respectively). Function did not improve significantly following quadriceps strengthening in either alignment group but there was a significant improvement in knee pain in the more neutral group only (P < 0.001).

Conclusions: Quadriceps strengthening did not have any significant effect on the KAM in participants with either more varus or more neutral alignment. The benefits of quadriceps strengthening on pain were more evident in those with more neutral alignment. Knee alignment thus represents a local mechanical factor that can mediate symptomatic outcome from exercise interventions in knee OA.

**CURCUMIN (DIFERULOYLMETHANE) BLOCKS DUROLANE PROVIDES ANTI-NOCICEPTIVE EFFECTS IN A MODEL OF ORAL AVACADO/SOYBEAN UNSAPONIFIABLES USING AN EXPERIMENTAL MODEL OF EQUINE OSTEOARTHRITIS**

A.L. Clutterbuck1, A. Mobasheri1, T.C. Rogers3, J. Wiseman2, D. Allaway3, P. Harris3. 1School of Veterinary Medicine and Science, University of Nottingham, Nottingham, UNITED KINGDOM. 2School of Biosciences, University of Nottingham, Nottingham, UNITED KINGDOM. 3WALTHAM Centre for Pet Nutrition, Melton Mowbray, UNITED KINGDOM

Purpose: Curcumin is the principal biologically active component of turmeric (Curcuma longa). Although it has been extensively investigated for its anti-tumor, antioxidant and anti-inflammatory properties in various cell models, few studies have explored its potential for counteracting inflammatory and catabolic pathways in articular cartilage. Curcumin has been shown to suppress the NFκB pathway and protect isolated human chondrocytes from the catabolic effects of IL-1β. The aim of this study was to see if curcumin could reduce glycosaminoglycan (GAG) and prostaglandin E2 (PGE2) release from explants of equine articular cartilage incubated with recombinant equine IL-1β in an in vitro model of inflammatory OA.

Methods: Normal articular cartilage was obtained from weight bearing regions of the metacarpophalangeal joints of three horses euthanized normally and that the pain inducing agents were not causing intolerable pain in the joints. This study has sought to evaluate the effect of Durolane in an in vivo model of joint pain.

Results: Curcumin significantly reduced IL-1β-stimulated GAG release in the explants at 50 μM (P < 0.05), 75 μM (P < 0.001) and 100 μM (P < 0.001). PGE2 release in response to IL-1β exposure was diminished by curcumin at 25μM, 50μM, 75μM and 100 μM (P < 0.001).

Conclusions: This study demonstrates that micromolar concentrations of curcumin exert significant anti-catabolic and anti-inflammatory effects in our inflammatory model of OA. These results support the use of this cartilage explant model as a screening assay for novel functional ingredients.

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**DUROLANE PROVIDES ANTI-NOCICEPTIVE EFFECTS IN A MODEL OF ARTICULAR JOINT PAIN**

M. Botter1, H-G. Schaitdle1, A.J. Harrison2. 1Klinikum der Friedrich-Schiller Universität, Jena, GERMANY. 2Smith & Nephew Group Research Centre, York, UNITED KINGDOM

Purpose: The degenerative joint disease, osteoarthritis (OA), is characterised with a loss of cartilage and increased pain from affected joints. It is this chronic pain which most patients associate with their condition. Non-steroidal anti-inflammatory drugs (NSAIDs) are used to treat inflammation and as a knock on effect, through the reduction of COX2 and prostaglandin E2 (PGE2), can reduce the pain associated with OA. However, NSAIDs are generally administered systemically and can exhibit harmful side effects. Hyaluronans have also been shown to reduce the pain associated with OA both in animal models and in clinical trials. Applied locally hyaluronans target the disease in the affected limb, further more the frequency of side effects of hyaluronans is considered to be low and are generally not serious in nature. There are a number of purified hyaluronans available and in recent years hyaluronan hydrogels, where the material has been crosslinked into networks, have become available. One of these crosslinked hyaluronan hydrogels is Durolane™. This study has sought to evaluate the effect of Durolane in an in vivo model of joint pain.

Methods: The model utilized the pain inducing substances bradykinin & PGE2 administered intra-articular (IA) and unilaterally into the knee joints of adult female Lewis rats. Rats were randomly allocated to one of three groups, Durolane, saline or morphine. The saline and Durolane (20 mg/ml) groups were injected IA (50 μl) once (Day 1), 2−4 hours before the first injection of bradykinin (182.25 μg) and PGE2 (0.5 μg) into the rat knee. The administration of the pain inducing agents was approximately 45 minutes before initiation of behavioural testing on each testing day. The morphine acted as a positive control and was administered at 2.5 mg/kg subcutaneously 30 minutes after bradykinin/PGE2 on each testing day. Behavioural testing was performed at 2 hours and 1, 2, 4, 7, 14, 21 and 28 days and included the assessment of mechanical thresholds at the knee, weight bearing and locomotor coordination on a rotarod.

Results: Mechanical thresholds at the knee were significantly decreased in saline treated animals. However, a single IA injection of Durolane on day 1 revealed similar anti-nociceptive effects as did the subcutaneous injection of morphine on each testing day until the end of the observation period at day 28. Significant differences between saline and Durolane were seen at days 1, 2, 4, 14 and 28. The incapacity test showed that animals treated with Durolane favoured a more 1:1 weight bearing between treated and untreated limbs. This result was again similar to those receiving a daily injection of morphine, whereas those treated with saline favoured the untreated limb, i.e. protecting the injected limb. Significant differences were seen at days 1, 2 and 14 between the saline and Durolane groups. Rotarod parameters indicating locomotive function were not significantly altered from baseline measures with any of the treatments administered. This demonstrates that animals could walk normally and that the pain inducing agents were not causing intolerable pain in the joints.

Conclusions: This study has demonstrated that a single IA injection of Durolane provides anti-nociceptive effects until at least day 28, in this model of induced joint pain.

**EVALUATION OF ORAL AVACADO/SOYBEAN UNSAPONIFIABLES USING AN EXPERIMENTAL MODEL OF EQUINE OSTEOARTHRITIS**

D.D. Frisbie, C.E. Kawcak, C.W. McIlwraith. Colorado State University, Fort Collins, CO, USA

Purpose: Joint disease and specifically osteoarthritis (OA) is one of the most prevalent and debilitating diseases affecting horses and humans.
EVALUATION OF BONE MARROW DERIVED STEM CELLS to evaluate ASU. Further research both using in vitro and clinical trials should be undertaken. Productstested usingthesamemodel of equine OA. Thesedatasuggest glycosaminoglycan and intravenous hyaluronan) and oral (hyaluronan) more than has been seen with some other parenteral (Polysulfated). They appeared improved. When ASU and Placebo treatments were compared although numerically significant increase in all of the pivotal parameters. Neither horses receiving BDMS or ADSVF in their OA joints showed any significant improvement in any of the same pivotal parameters except PGE2 which was significantly decreased in BDMS treated horses. Conclusions: The results of the current study and Murphy et al. combined suggest that the regeneration of the medial meniscus in Murphy et al.’s study may have in fact been the reason for less OA progression. Furthermore, the current study also suggests that MSC’s by themselves do little to counteract the progression of OA mediated by enzymatic degradation and joint debridexcept for decreasing PGE2. It would appear modification of the MSC’s is needed if they are to be clinically useful in treating the OA represented in the current model.

519 EVALUATION OF BONE MARROW DERIVED STEM CELLS AND ADIPOSE DERIVED STROMAL VASCULAR FRACTION FOR TREATMENT OF OSTEARTHRITIS USING AN EQUINE EXPERIMENTAL MODEL.

D.D. Frisbie, C.E. Kawcak, N.M. Werpy, C.W. McIlwraith. Colorado State University, Fort Collins, CO, USA.

Purpose: Joint disease and specifically osteoarthritis (OA) is one of the most prevalent and debilitating diseases affecting both humans and horses. While claims that adipose derived stem cells improve horses with clinical OA, no controlled clinical studies have been published in horses to date. Furthermore no controlled studies have been published on bone marrow derived stem cells for the treatment of OA in either humans or horse OA. Bone marrow derived stem cells expanded in culture have been used to regenerate and/or repair a variety of tissues but to date only one study has been published evaluating the in vivo effects of intraarticular stem cell injection on decreasing the progression of experimental OA in a goat model of OA. This study used a medial meniscectomy and cranial cruciate transaction model to induce OA. The decrease in OA seen in the study was thought to be secondary to the regeneration of the medial meniscal tissues, which was dramatic in 7 of 9 cases. The design of the study did not lend itself to determining if the stem cells had a direct effect on the articular cartilage. Based on unpublished data there is some evidence that stem cells have a tropism for fibrillated articular cartilage. This coupled with the overwhelming capacity of stem cells for regeneration of many tissue types, the current study was undertaken. Unlike the study by Murphy et al., the model used in this current study does not rely on joint instability (medial meniscal model) to create secondary OA but rather an osteochondral fragment in concert with articular cartilage and bone debris created at the time of fragmentation. It is believed that the progression of OA in this model is largely enzymatically and particle mediated.

Methods: This study was a blinded experimentally controlled randomized block design that utilized 16 horses in an established model of osteoarthritis. On day 0 of the study, arthroscopic surgery was performed, and OA was induced unilaterally in the mid-carpal joint of all horses. On day 0, horses were divided into two treatment groups: placebo control and ASU treated. The placebo control horses (n = 8) received molasses orally once daily, while the ASU treated horses (n = 8) received 8g of ASU plus a similar volume of molasses orally, both treatments were continued throughout the study period. On day 14 horses began and continued treadmill exercise for the remaining 8 weeks of the study. Synovial fluid and serum were assessed every other week for total protein concentration, white blood cell count (WBC) and levels of the inflammatory marker, prostaglandin E2 (PGE2). Horses were assessed for lameness using the AAEP grading scale every two weeks. At the termination of the study, operated joints were evaluated grossly, and tissues were harvested for biochemical and routine histologic examinations.

Results: All horses completed the study and no adverse events were recorded. At the termination of the study horses treated with ASU were observed to have significantly improved total gross examination score (articular cartilage erosion + synovial membrane hemorrhage score) in their OA joint when compared to placebo treated horses. The degree of lameness and other outcome parameters were not significantly different when ASU and Placebo treatments were compared although numerically they appeared improved.

Conclusions: While the significant improvements were modest, it is more than has been seen with some other parenteral (Polysulfated glycosaminoglycan and intravenous hyaluronan) and oral (hyaluronan) products tested using the same model of equine OA. These data suggest further research both using in vitro and clinical trials should be undertaken to evaluate ASU.

520 EVALUATION OF AUTOLOGOUS CONDITIONED SERUM USING AN EXPERIMENTAL MODEL OF EQUINE OSTEOARTHRITIS

D.D. Frisbie, C.E. Kawcak, C.W. McIlwraith. Colorado State University, Fort Collins, CO, USA.

Purpose: Interleukin-1 (IL-1) is thought to be the major mediator of joint disease. Studies in both humans and horses have evaluated the use of a natural antagonist (interleukin-1 receptor antagonist, IL-1Ra) to block IL-1 and decrease the progression of joint disease.

A novel product to the United States has been introduced for the treatment of equine OA, autologous conditioned serum (ACS). This product has been shown to stimulate the production of IL-1Ra from cultured peripheral blood of human patients by 140 fold. The purpose of this study was to evaluate ACS compared to placebo treatment using a horse model of OA.

Methods: This study was a randomized blinded controlled study that utilized 16 horses in an established model of osteoarthritis. On day 0 of the study, arthroscopic surgery was performed, and OA was induced unilaterally in the mid-carpal joint of all horses. On day 14, horses were divided into two treatment groups: placebo control and ACS treated. The placebo control horses had 6ml of saline injected into the OA joint on days 14, 21, 28 & 35 while the ACS treated joints (OA joints) received 6ml of serum prepared as directed by the manufacturer at similar time periods. On day 14 the horses began a strenuous exercise regime 5 days per week for the remaining 8 weeks of the study. Synovial fluid and serum were assessed every other week for total protein concentration, white blood cell count (WBC) and levels of the inflammatory marker, prostaglandin E2 (PGE2). Horses were assessed for pain using a standardized scale every two weeks. At the termination of the study, operated joints were evaluated grossly, and tissues were harvested for biochemical and routine histologic examinations.

Statistical analysis utilized an analysis of variance and a Least Square mean for individual comparisons, p-values <0.05 were considered significant.

Results: All horses completed the study and no adverse events. ACS processed serum had a significant increase in IL-1Ra concentrations when compared to control serum (234±27 versus 45±29 pg/mL, respectively). Horses treated with ACS were observed to have significantly improved lameness in OA joints, even five weeks after the last treatment when compared to placebo treated horses (1.3±0.2 versus 2.1±0.2, respectively). A significant reduction in synovial membrane hyperplasia was also seen in the treated compared to placebo OA joints at day 70 (0.4±0.3 versus 0.3±0.3, respectively). The levels of IL-1Ra were also significantly elevated in the joints of ACS treated horses after day 35 and were estimated to be 71±13 versus 44±13 pg/mL on day 70 when treated versus placebo synovial fluid was compared respectively.

Conclusions: The ACS system used here stimulates peripheral white blood cells to produce an “anti-inflammatory soup”. An import finding of this study was to note the side effects associated with the intraarticular administration of ACS. Significant clinical improvement was seen following treatment of induced OA at the last point measured during the study. Significant improvement was also noted in synovial membrane parameters, as well as trends for gross improvement, further supporting a therapeutic