

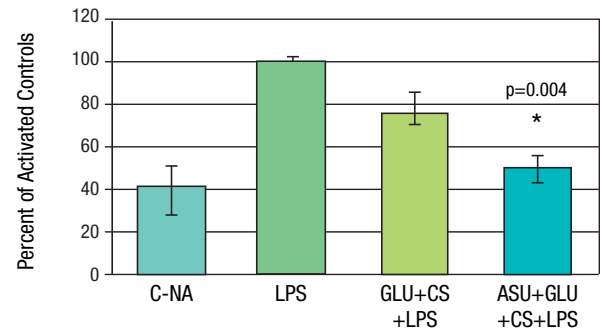
# SUPERIOR JOINT HEALTH SUPPLEMENTS ALWAYS BACKED BY RESEARCH

- The combination of avocado/soybean unsaponifiables (ASU) and glucosamine/chondroitin sulfate (GLU/CS) profoundly suppressed COX-2 production in Lipopolysaccharide (LPS)-activated equine chondrocytes (see figure 1). The combination was more effective than either was alone.<sup>1</sup>
- The combination of hyaluronic acid (HA) and ASU/GLU/CS significantly lowered PGE<sub>2</sub> production in IL-1 $\beta$ -stimulated equine chondrocytes (see figure 2); effects were better than HA or ASU/GLU/CS alone. The decrease in PGE<sub>2</sub> production was associated with inhibition of the translocation of NF-KB, a mediator that helps “switch on” the inflammatory response.<sup>2</sup>
- Another study showed that ASU and EGCG (epigallocatechin gallate, an extract from green tea) significantly decreased COX-2 expression (see figure 3) and PGE<sub>2</sub> production in cytokine-activated equine chondrocytes. The combination was better than either agent alone. As above, effects were associated with inhibition of NF-KB translocation (see figure 4).<sup>3</sup>

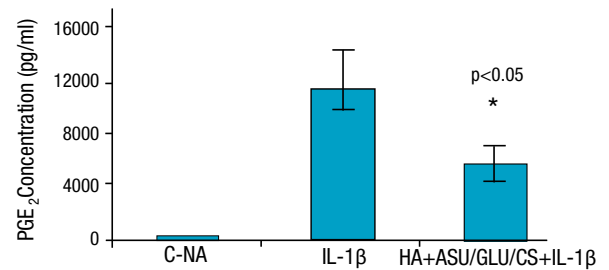
**These in vitro studies show that the ingredients in COSEQUIN ASU and COSEQUIN ASU PLUS inhibit production or expression of numerous mediators along the inflammatory cascade.**

***The use of COSEQUIN ASU and COSEQUIN ASU PLUS may be beneficial to provide joint health protection when other modalities are used***

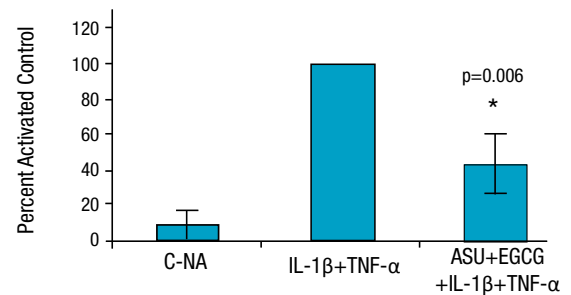
- Addition of enrofloxacin to equine chondrocyte cultures was shown to up-regulate PGE<sub>2</sub> production. This increase was inhibited by the combination of ASU/GLU/CS.<sup>4</sup> **So while intra-articular administration of an antibiotic may be needed to treat infection, ASU/GLU/CS may help minimize any effects it may have on cartilage.**
- Inflammatory mediators caused increases in PGE<sub>2</sub> production and activation of matrix metalloproteinase-9 (MMP-9), an enzyme that breaks down cartilage, in equine chondrocytes. Adding phenylbutazone to the cultures decreased PGE<sub>2</sub> production as expected, but phenylbutazone and ASU/GLU/CS together also decreased MMP-9 activation.<sup>5</sup> **Based on these results, administration of ASU/GLU/CS when using phenylbutazone may help to maximize attenuation of both inflammatory mediators and enzymes, which all play a role in cartilage breakdown.**



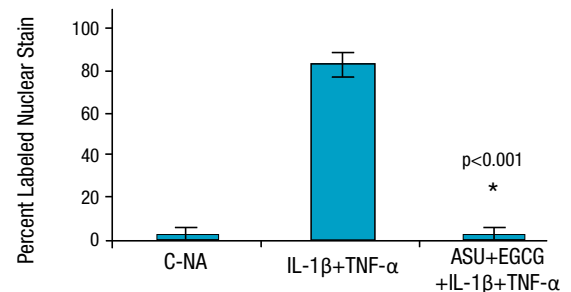
**Figure 1: Combination of ASU and GLU/CS inhibits COX-2 in equine chondrocytes. (C-NA=non-activated control) (\*=statistical significance relative to GLU+CS+LPS)**



**Figure 2: Combination of HA and ASU/GLU/CS inhibits PGE<sub>2</sub> production in equine chondrocytes. (C-NA=non-activated control) (\*=statistical significance relative to IL-1 $\beta$ )**



**Figure 3: Combination of ASU and EGCG inhibits COX-2 expression in equine chondrocytes. (C-NA=non-activated control) (\*=statistical significance relative to IL-1 $\beta$ +TNF- $\alpha$ )**



**Figure 4: Combination of ASU and EGCG inhibits nuclear translocation (activation) of NF- $\kappa$ B. (C-NA=non-activated control) (\*=statistical significance relative to IL-1 $\beta$ +TNF- $\alpha$ )**

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#### REFERENCES:

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5. Dougherty JJ, Heinecke LF, et al. Effect of phenylbutazone and the combination of avocado soybean unsaponifiables, glucosamine and chondroitin sulfate on metalloproteinase activity in equine chondrocytes, in Proceedings. 2009 ACVS Symposium;xxxi-xxxii.

†Source: Survey conducted in February 2014 of equine veterinarians who recommended oral joint health supplements.

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