

# Protecting a Horse's Health with a Resveratrol Analogue, Antioxidants and Curcumin

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The role of inflammation and oxidative stress in cellular injury and the pathogenesis of many acute and chronic illnesses is a major area of attention and research. Many disorders in both humans and animals have been directly linked to inflammation and oxidative stress. Indeed, it is impossible to separate the two due to their intricately linked reactions. Certain events that initiate inflammatory and oxidative stress responses can be avoided; however, for most of us, and particularly for the horse, there is the certainty that one will always be confronted with these stressors to some degree. Due to the ubiquitous nature of inflammatory and oxidative stressors, it is imperative to prevent exacerbation or prolongation of the body's responses, as they can ultimately result in poor performance, metabolic disturbances, and decreased quality of life. Various dietary strategies have been designed to combat inflammatory and oxidative insults. For example, anti-inflammatory diets, such as one that is relatively high in omega-3 fatty acids and low in omega-6 fatty acids, are often advocated for healthy living. However, other nutrients can play a significant role in controlling inflammation and oxidative stress.

## Phytonutrition

**Pterostilbene** is a compound that is chemically very similar to resveratrol, which received much public and scientific attention in past years for its purported ability to increase lifespan as well as protect against various diseases and conditions.<sup>1</sup> Unfortunately, resveratrol has limited potential due to its poor bioavailability and/or very quick degradation once it is absorbed. However, as a methylated analogue of resveratrol, pterostilbene is far more promising. For example, oral intake studies indicate that pterostilbene is 70-90% bioavailable whereas resveratrol has a 20-30% absorption rate.<sup>2,3</sup> Furthermore, pterostilbene remains intact in the blood for up to 7 times longer than resveratrol.<sup>4</sup> Biological activities attributed to pterostilbene range from analgesic, anti-inflammatory, antioxidant anti-diabetic, anti-obesity, anti-micotic, anti-cancer, anti-aging, vascular health supporting and neuroprotective effects.<sup>3,5-9</sup> The mechanisms of action attributed to pterostilbene include both modulation of gene expression and enzymatic activity.<sup>10</sup> Rats supplemented with pterostilbene have increased activity of the

antioxidant enzymes: superoxide dismutase, glutathione peroxidase, and catalase.<sup>11</sup> These changes were accompanied by a decrease in oxidized lipids, as well. Alterations in gene expression induced by pterostilbene have included reductions in MMP-3 (an extracellular degradative enzyme), TNF-alpha (a systemic inflammatory protein) and the enzyme COX-2, which is responsible for the production of multiple pro-inflammatory factors.<sup>11,12</sup>

## Antioxidants

**Superoxide Dismutase (SOD)** is a metalloenzyme that is present in nearly all cells where it catalyzes the dismutation of superoxide to oxygen and hydrogen peroxide. Although the importance of SOD in modulating oxidative stress has been well understood for years, few trials have reported on the benefits of oral supplementation with this enzyme until relatively recently. To date, improvements in self-perceived fatigue,<sup>13</sup> increased activities of circulating antioxidant enzymes and red blood cell resistance to hemolysis,<sup>14</sup> and reductions in intestinal tract stress proteins<sup>15</sup> have

been reported in humans and animals. In the horse, oral supplementation for 60 days with a melon extract high in SOD during intense training was associated with maintenance of resting plasma levels of creatine kinase,<sup>16</sup> an enzyme that is often increased after muscle damage associated with exercise. Furthermore, plasma resistance to hemolysis improved in the supplemented group and was significantly greater than that in the control group.

Other antioxidants, such as vitamins E and C, have also been utilized as oral supplements to aid in the protection against oxidative stress and inflammation. **Vitamin E** has been negatively correlated with levels of certain markers of lipid peroxidation in exercising horses,<sup>17</sup> and **vitamin C** supplementation has been shown to reduce markers of lipid peroxidation and maintain plasma antioxidant capacity in thoroughbred race horses.<sup>18</sup> The combination of vitamins E and C have been utilized to treat horses with recurrent airway obstruction.<sup>19</sup>

### Curcumin

The benefits of curcumin, which is the primary active ingredient of turmeric, have had a prominent role in Indian Ayurvedic medicine since 1900 BC.<sup>20</sup> Curcumin purportedly has anti-inflammatory, hepato-protective, antioxidant, and anti-carcinogenic properties<sup>21</sup> and is a suggested therapeutic agent for inflammatory conditions such as inflammatory bowel diseases, pancreatitis, and arthritis,<sup>21</sup> as well as cognitive disorders.<sup>22</sup> Curcumin's biochemical benefits are due, in part, to regulation of transcription factors such as PPARgamma and NF-kappa beta.<sup>22,23</sup> The resultant improvements in cytokine and inflammatory markers is demonstrated by reductions in TNF-alpha, IL-1beta, IL-6 and the COX-2 and LOX enzymes.<sup>21</sup> Franck *et al.*<sup>24</sup> studied curcumin's effect on inflammation in horses by stimulating equine neutrophils and then measuring production of oxidative products, a reaction associated with diseases such as laminitis, recurrent airway obstruction, and endotoxic shock.<sup>25-27</sup> These investigators reported a dose-dependent inhibition of curcumin on reactive oxygen species production and myeloperoxidase activity. Another *in vitro* study showed that curcumin protects equine cartilage

explants against IL-1beta induced degradation.<sup>28</sup>

### Feeding Trial

The aforementioned nutrients all have antioxidant and anti-inflammatory properties that make them ideal candidates for a broad-spectrum supplement designed to address the consequences of daily living stresses, including those due to intense exercise, poor-quality nutrition, or simply the aging process. Researchers with the Alamo Pintado Center for Biological Medicine conducted a feeding trial that characterized biochemical changes in clinically healthy horses before and after supplementation with such a combination product.\* Four horses were supplemented twice daily with a paste containing pterostilbene, superoxide dismutase, antioxidant vitamins, and curcumin. Two horses served as controls. All horses were maintained on an oat and alfalfa hay diet plus a small amount of corn oil. Horses were maintained in individual stalls and exercised 3 to 4 times each week for 20-30 minutes. Fasting and post-prandial blood samples were obtained from all horses at the start of the trial and three and seven weeks later for analysis of inflammatory and oxidative stress markers.

No significant differences existed between groups at the start of the trial. After seven weeks of supplementation, there was a significant decrease in expression of genes for the pro-inflammatory markers: IL-1beta, TNF-alpha, and IL-6. No change was noted in the control group (Figures 1-3). Although no statistical difference was noted between the values at the start of the trial and week 7 in the expression of the COX-2 enzyme, there was a significant reduction when values at week 7 were compared to those at week 3 (data not shown). The lack of significance from the value at the start of the trial likely was due to the unusually high level of variation at that time in this marker. A 31% decrease in post-prandial protein carbonyls, a measure of oxidized proteins, was noted in the supplemented group after three weeks of supplementation; no change was noted in the control group (Figure 4). Post-prandial protein carbonyls in the supplemented horses were also significantly lower than the fasting values at week 3; no change was noted in the control group (data not shown). Another marker of oxidative damage is thiobarbituric acid reactive substances (TBARS), which

\*Platinum Longevity®

represents oxidized lipids. Based on changes in TBARS in the supplemented horses, lipid peroxidation in fasting blood samples was significantly reduced from week 3 to week 7 (Figure 5). No such change was noted in the control group (data not shown).

Figure 1. **IL-1beta Gene Expression Following 7 Weeks of Supplementation\* vs Control Horses**

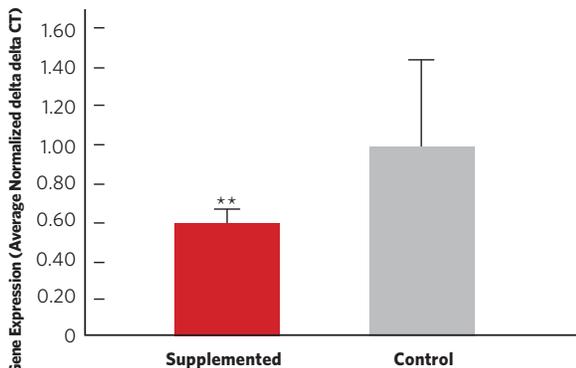


Figure 2. **TNF-alpha Gene Expression Following 7 Weeks of Supplementation\* vs Control Horses**

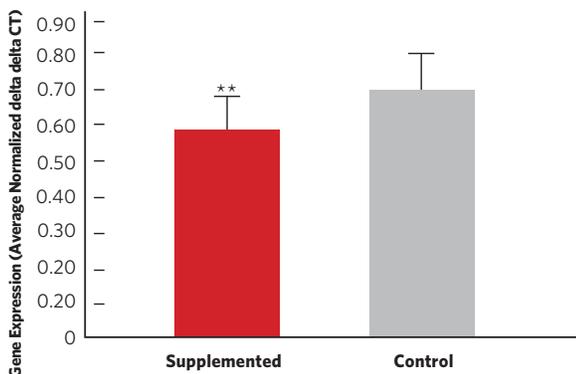


Figure 3. **IL-6 Gene Expression Following 7 Weeks of Supplementation\* vs Control Horses**

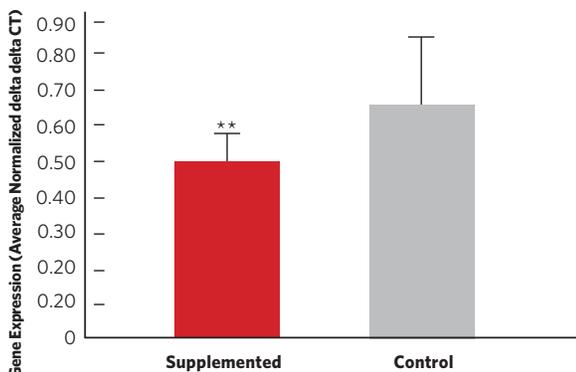


Figure 4. **Post-Prandial Damaged Protein Content in Blood**

**Before and After 3 Weeks of Supplementation\* vs Control Horses**

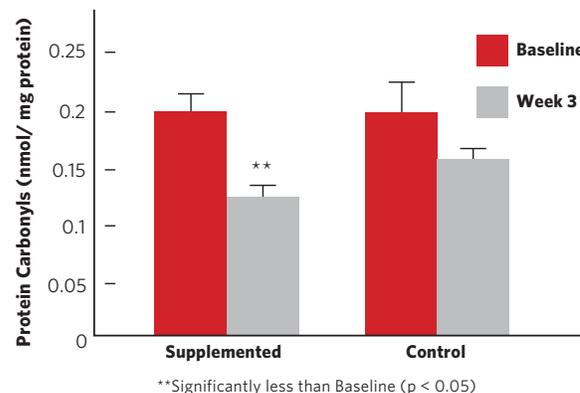
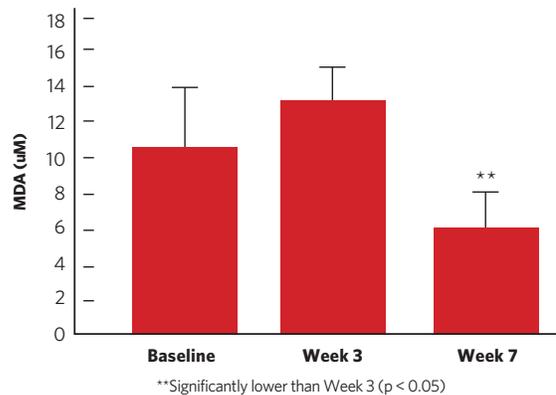


Figure 5. **Damaged Lipids in Fasting Blood Following Supplementation\***



## Summary

The results of this preliminary trial indicate that supplementation of horses with a combination of pterostilbene, superoxide dismutase, antioxidant vitamins, and curcumin, significantly reduces measures of inflammation and oxidative stress. Recognizing that these conditions are directly linked to several equine diseases, daily provision of these nutrients can be a critical component of your horse's diet, whether he is in competition, dealing with stresses of a pre-existing illness, or is experiencing the effects of aging.

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