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Ergogenics & Supplements for performance horses: recent innovations

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Ultimately, we provide nutritional supplements to our horses because we perceive that there are nutrient deficiencies that are preventing our horses from achieving the goals that we have set for them. Nutritional and nutraceutical supplements capture a category of products that has seen explosive growth in the past decade. Previously reserved for those attempting to fine-tune their classical nutrition programs, nutraceutical supplement has boldly crossed over the threshold of nutrition and into that of promotion of robust health and performance enhancement, beyond that provided by simple sound nutrition. The nutraceuticals industry is bolstered by a growing desire to push past the limitations of classical and training and feeding, and find that 'extra edge' that encourages a faster race, a higher jump, a more expressive piaffe.

Until recently, the main research focus on nutritional supplements for horses has been on macronutrients such as carbohydrates, fats and protein or amino acids. There has also been a substantial research effort directed at trace minerals and electrolytes and their ability to improve health and performance. Nonetheless, when we have a high degree of certainty that we have fully, or at least adequately addressed these needs, we sometimes find that our horses still do not reach their genetic and/or physiological potential. We therefore continue to examine other strategies for improving wellness and performance. We want our horses to be able to achieve performance at a level that equals their genetic potential.

An increasing trend in recent research is to examine the effects of nutraceuticals or functional foods. These are typically mixtures of single animal or plant components, or blends of such mixtures, that are believed to exert wellness benefits that cannot be readily attributed to macronutrients and micronutrients. These products typically comprise a vast array of bioactive molecules that interact with numerous biochemical and signaling pathways in virtually every cell system within the body. The plant and animal parts from which these nutraceutical products are derived tend to have a long history of use in human and animal folklore medicine. At the same time we have a poor understanding of these products because of their complex nature and myriad interactions. We are only at the beginning of a long path of discovery, research and more discovery.

A paradigm for describing the interplay between nutrients, stress and function is shown in Figure 1. Inadequate provision of nutrients contributes to stress

because cellular / tissue demand for certain nutrients are not being met. The cells / tissues / organisms will either adapt or break down. Inflammation, when controlled, is a normal and essential part of the adaptation process. It is when inflammation is relatively uncontrolled that breakdown occurs and we become very concerned.

In this review we focus on a few newer nutraceutical approaches that are aimed at dealing with the oxidative stress and inflammation that accompanies physiological strain, with an emphasis on exercise strain (Figure 2). In this context strain is taken as excess stress, where it is recognized that stress is normal and unavoidable and indeed a requirement for cellular, tissue, organ and organism adaptation. Excess acute stress, as well as chronic stress, imposes severe demands upon the stressed systems within our bodies and is an important contributor to unwellness and poor performance. Can nutraceuticals be used to prevent or minimize excess stress and strain?

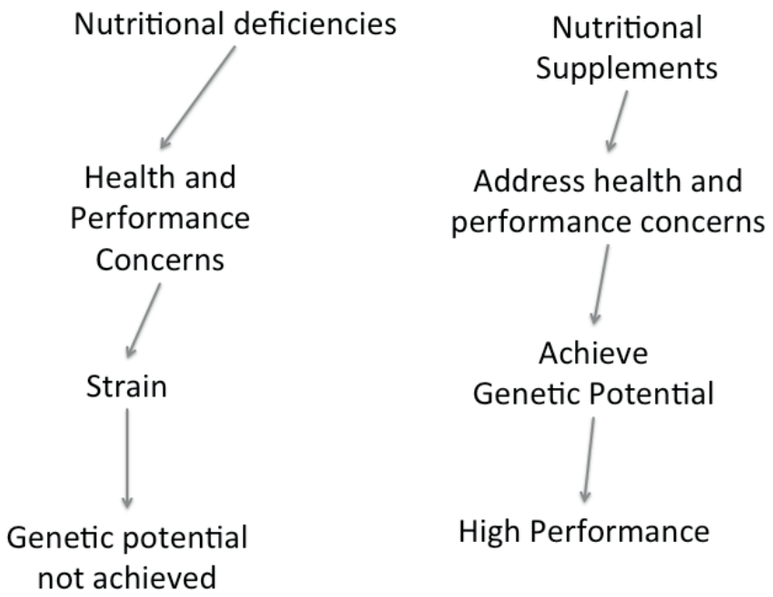

Figure 1. The left side depicts a paradigm indicating the relationship between nutritional deficiencies (i.e. nutrient supply is not adequate to meet nutrient demand) and poor athletic performance such that the horses is not able to achieve its genetic potential. The right side shows that genetic potential may be achievable when nutrient supply meets nutrient demand, such as to avoid health and wellness concerns.

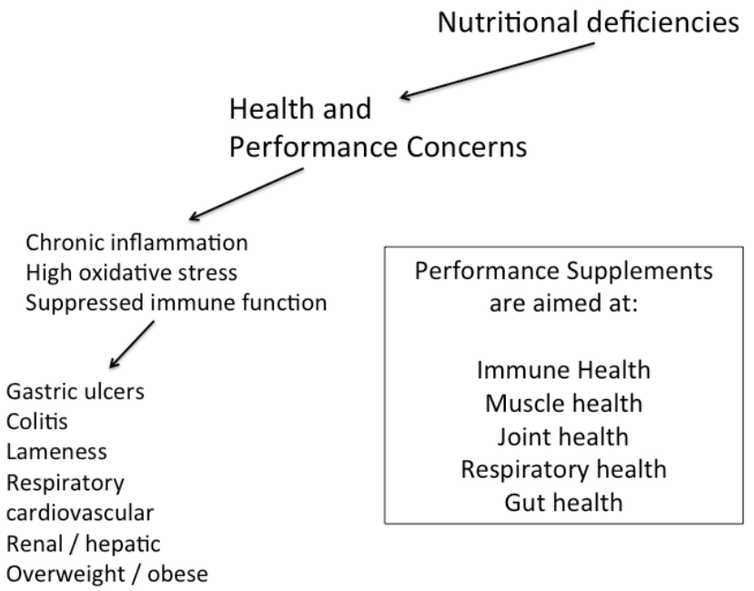

Figure 2. Nutritional deficiencies contribute to a number of pathologies that are often a result of chronic inflammation, high oxidative stress and suppressed immune function. Deficiencies can be addressed through improved nutrition.

For example, repeated bouts of high intensity exercise, taking place within a single training session, or even spread over months of training sessions, can result in strain. Within a single training session we now know that repeated bouts of high intensity exercise past an as yet poorly recognized and defined threshold, results in cellular strain. Cellular strain will be manifest in exercising muscle as increased oxidative stress resulting from high rates of production of reactive oxygen species (ROS) or oxygen free radicals. Under normal conditions, cells are able to prevent excessive and prolonged increases in ROS through the actions of enzymes capable of degrading ROS. When rates of ROS production exceed rates of ROS degradation, the continued and sometimes prolonged oxidative strain results in destruction of cell membranes, leading to cell death (apoptosis) and tissue destruction. This presents itself to us as inflammation (Lugrin *et al*. 2014) and the pain, soreness, unwellness and impaired performance associated with tissue destruction (Figure 3). When the affected tissue is skeletal muscle, we see the effects in blood plasma as elevated concentrations of muscle-specific enzymes such as creatine kinase (CK), aspartate aminotransferase (AST) and lactate dehydrogenase (LDH) (Billings 2014). The concentrations rise after cessation of exercise and the peak is proportional to the magnitude of muscle damage (Lamprecht *et al*. 2009).

In horses, oxidative stress occurs during intense exercise (Chiaradia *et al*. 1998; White *et al*. 2001; de Moffarts *et al*. 2004) and endurance exercise (Marlin *et al*. 2002; Williams *et al*. 2005, 2004). It is also recognized that muscle membrane leakage occurs in horses when oxidative stress is high, as occurs with endurance exercise (Hargreaves *et al*. 2002; Williams *et al*. 2004).

There is interplay between oxidative stress, inflammation and immune function (Figure 3) that has important implications for how, and what we feed our horses, and when best to exercise train and compete our horses. For example, it is now well known that exercise causes significant changes to various immune cell parameters, particularly cells of the innate immune system (macrophages, natural killer (NK) cells and neutrophils). Elevated respiratory activity of skeletal muscle cells (moderate and high intensity exercise) increases the mitochondrial production of superoxide (O_2^-) that is acted on by superoxide dismutase (SOD) resulting in the production of another ROS, hydrogen peroxide (H_2O_2). If muscle becomes inflamed as a result of the activity, neutrophil numbers and H_2O_2 production by neutrophils is increased, particularly with increased frequency of neutrophil respiratory burst activity and phagocytic activity. Exhaustive exercise, however, may suppress the functions of innate immune cells (Sureda *et al*. 2007; Donovan *et al*. 2007; Echigoya *et al*. 2012).

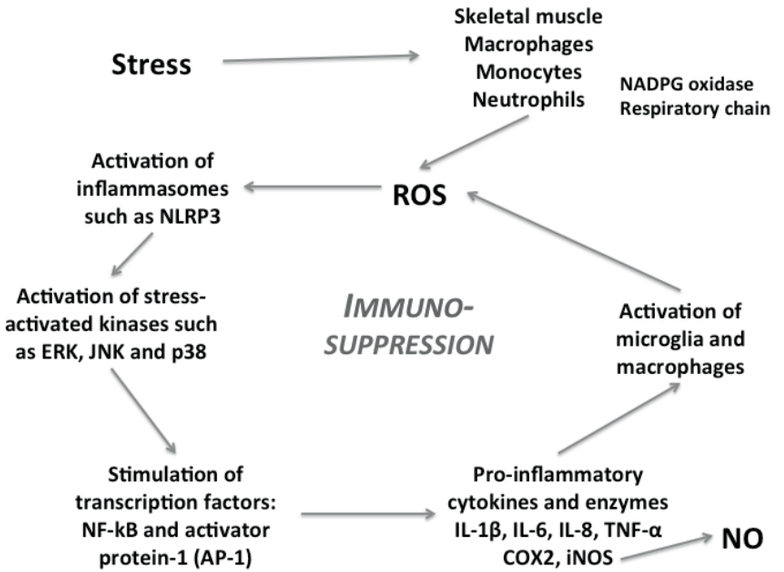

Figure 3. Stress within cells and tissues leads to oxidative stress and inflammation. When controlled, these are normal and essential parts of beneficial tissue adaptations. When uncontrolled, or when stress is excessive, then excessive inflammation, pain and tissue damage will occur, leading to prolonged periods of unwellness and poor performance.

From the preceding paragraphs, and the following one, it is apparent there are two phases to the oxidative stress and inflammation of acute, intense exercise. This first results from the exertion itself, while the second is a response to the damage caused by exertion (below).

In animal studies, strenuous exercise that results in muscle microtrauma (ultrastructural damage) is characterized leukocyte infiltration and an inflammatory response resulting from oxidative stress (Michailidis *et al*. (2013). Part of the healing process to microtrauma involves the inflammatory response that occurs in response to the damage. The infiltration of leukocytes into damaged regions of the muscle fiber exerts antiseptic protection by releasing (ROS) through activation of NADPH oxidase (respiratory burst). Cytokines released by damaged muscle fibers and infiltrating neutrophils further activate ROS-generating enzymes (xanthine oxidase, COX-2). In the controlled state, an elevation of endogenously produced antioxidants maintain the inflammatory response under some control. When poorly controlled, sustained high ROS may cause secondary damage to injured and noninjured fibers. Reduced glutathione (GSH) is another potent antioxidant that is converted to its oxidized form (GSSG), ratio or redox potential of muscles. These pathways also impact on redox-sensitive signaling cascades important in the transcriptional activities involved in immune cell recruitment, adhesion molecule mobilization, antioxidant synthesis, and satellite cell recruitment. Key regulators in these pathways are nuclear transcription factor kB (NF-kB), mitogen activated protein kinases (MAPK), and protein kinase B (Akt)/ mammalian target of rapamycin (mTOR) (Michailidis *et al*. 2013).

Supplements aimed at reducing oxidative damage - antioxidants

It may be evident from the preceding description that a nutritional supplement that prevents or reduces the oxidative stress associated with intense exercise should reduce the amount of skeletal muscle damage that occurs, with attendant reductions in inflammation and pain, and with improved post-exercise recovery (Figure 4). An effective supplement could translate to improved next-day performances (i.e. stadium jumping on the 3rd day of three-day eventing; multi-day endurance rides; daily sequences of high intensity training).

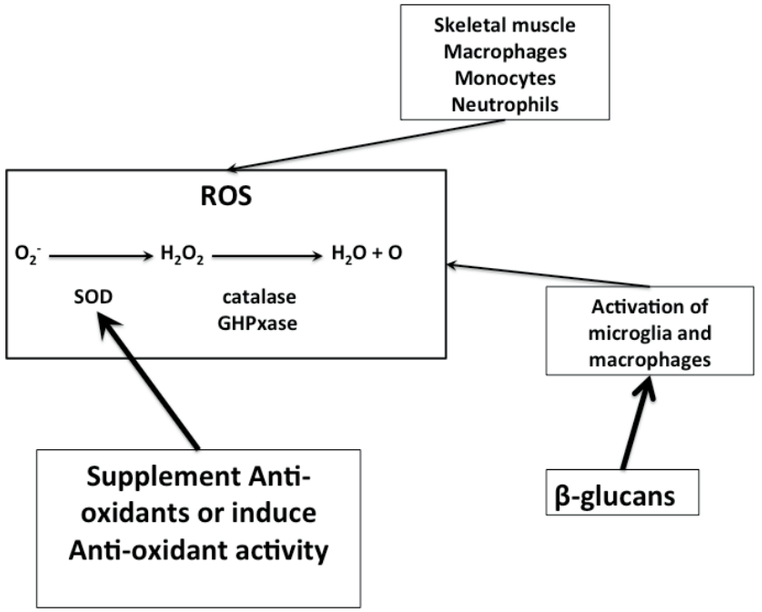

Figure 4. An example of how nutritional supplementation with antioxidants or beta-glucans may be able to provide some defense against oxidative stress and inflammation associated with high intensity and prolonged exercise. GHPxase = glutathione peroxidase

Superoxide dismutases (SODs)

SODs are produced by every living cell, reflecting its importance in the body to convert superoxide (O_2^-) radicals to less toxic oxygen (O_2) or hydrogen peroxide (H_2O_2). There are three main SOD isoforms in humans, found specifically within the extracellular fluid (SOD3), the cytoplasm (SOD1) and mitochondria (SOD2). It is appears that this arrangement is conserved in equids (Ishida *et al*. 1999). The various isoforms of SOD are important also because they play a role in the activation of two other anti-oxidant enzymes catalase and glutathione peroxidase, and signal other cells to increase production of SOD.

Researchers have investigated the hypothesis that oral SOD supplementation will reduce the severity of oxidative stress and damage associated with high intensity exercise. The hypothesis is based on a number of in vitro and in vivo studies showing that SOD reduces oxidative stress and inflammation (reviewed by Carillon *et al*. 2013). It needs to be noted that SOD, when not protected and orally supplemented, is not adequately bioavailable due to its low (14-22%) absorption into the circulation (Regnault *et al*. 1996) and rapid elimination by the kidneys (Carillon *et al*. 2013). A wheat gliadin encapsulated form has been developed, and the encapsulation preserves the SOD activity and is capable of eliciting in mice in vivo, and cells in vitro, the pharmacological effects consistent with SOD activity (Vouldoukis *et al*. 2004a, 2004b; Taoufiq *et al*. 2006).

The beneficial effects sometimes reported after oral supplementation with compounds that contain SODs (see below) cannot be explained on the basis of SOD activity of the ingested products. This is because a) orally supplemented SODs are very poorly absorbed, and b) the half-life of SODs is only a few minutes in plasma, observed decreases in oxidative stress and inflammation cannot be adequately explained by a direct effect of orally administered SODs. Carillon *et al*. (2013) have suggested that exogenous SODs have an additional influence independent of their antioxidant activity. They proposed an induction of endogenous antioxidant defense after exogenous SODs administration. A potential first step in such a mechanism would be a local, intestinal activation of the immune system inducing a cascade leading to the activation of macrophages systemically (Vouldoukis *et al*. 2004b). The exogenous SOD, as an antigen, could stimulate a protective immune response, which, in turn induces endogenous antioxidant defenses possibly via the upregulation of the transcription factor nuclear-factor-E2-related factor (Nrf2) Nrf2/ARE pathway (Carillon *et al*. 2013). Subsequently, the induction of antioxidant enzymes could be transcriptionally regulated through a putative antioxidant response element (ARE) (Nguyen *et al*. 2013; Carillon *et al*. 2013).

Notin *et al*. (2010) studied 2 groups of 12 Standardbreds in training. The SOD was in the form of a lyophilized, powdered melon encapsulated in polymeric wheat gliadin called Promutase 200 (Lallemand Animal Nutrition). The treatment group received 520 IU of SOD /day for 60 days and the placebo group received the excipient with no active substances. On days 0, 30 and 60 of supplementation the physiological responses to a standardized exercise test were assessed, including plasma creatine kinase, erythrocyte SOD, and blood resistance to haemolysis (KRL test). In the SOD group, 60 days of supplementation resulted in a significant increase in the plasma resistance to haemolysis. In the SOD group resting plasma CK remained unchanged, but increased in the placebo group. The authors concluded that oral SOD supplementation may make erythrocyte and muscle cells membranes less permeable during the stresses associated with regular exercise training.

Lamprecht and Williams (2012) evaluated the effect(s) of oral SOD supplementation in horses following intense exhaustive exercise. The SOD was also in an encapsulated form. Horses were fed 3000 IU SOD / day of powder for 6 weeks; they did not observe a benefit on blood and synovial fluid markers of inflammation (PGE_2, chondroitin sulphate; gene transcripts for interferon-gamma, interleukin-10, and interleukin-1β in blood, and decreased plasma nitric oxide) and antioxidant status (SOD, total glutathione, glutathione peroxidase) in response to a single bout of repeated sprint exercise test at 6 weeks.

It presently remains unknown why SOD, when administered to horses orally in encapsulated form at 520 IU for 60 days (Notin *et al*. 2010) or 3000 IU for 42

days (Lamprecht and Williams 2012) had only minor effects. It is possible that the isoforms of SOD used were not well absorbed by the g.i. tract or incapable of inducing the activities of endogenous antioxidant enzymes. It may be that it is not the exogenous SOD that is exerting the effects, but rather that any absorbed SOD, or even some other absorbed bioactive, is either directly or indirectly responsible for the effects (Carillon *et al*. (2013).

Other orally-supplemented antioxidants

While SOD can effectively regulate concentrations of superoxide, other antioxidants are required to regulate the concentrations of H_2O_2 produced in SOD reactions. Chief amongst these metabolites and enzymes are vitamin E, selenium, catalase and glutathione peroxidase. Glutathione peroxidase and catalase convert H_2O_2 to water (H_2O) and oxygen (O_2), with glutathione peroxidase having a greater affinity for, but decreased capability of, converting H_2O_2 than catalase. Catalase likely performs a greater role in stress situations, while glutathione peroxidase may be expected to perform more of a fine-tuning or housekeeping role. Both enzymes can be induced by increases in SOD activities (for review see Urso and Clarkson 2003). Vitamin C is a water soluble molecule that is an electron donor, and this accounts for its antioxidant activity when orally supplemented at relatively high doses (Padayatty *et al*. 2003). Vitamin E is a family of 10 related, though structurally distinct, lipid soluble molecules that function to protect cell membranes from oxidation by preventing ROS and lipid radicals from further reaction with lipid components of cell membranes (Traber and Atkinson 2007). Selenium is a non-metal, essential micronutrient in mammals that exerts its biological functions through selenoproteins. Selenoproteins contain selenium in the form of the amino acid selenocysteine, an analog of cysteine with selenium replacing sulphur. The human genome encodes at least 25 selenoproteins. Selenoproteins have stronger nucleophilic and electrophilic properties than cysteine, and are involved in redox systems and signaling pathways (Kurokawa and Berry (2013).

Deaton *et al*. (2002) used a mixture of antioxidants in the hopes of inducing synergistic interactions that would increase the ability to detect functional benefits. Horses were fed, for 4 weeks, a supplement of natural antioxidants together with selenium and vitamins C and E (Winergy Ventil-ate; MARS Horsecare UK Limited). It was hypothesized that 4 weeks of supplementation would increase the systemic and pulmonary antioxidant capacity, such that markers of oxidative damage would be decreased and pulmonary function during exercise improved. The supplement increased by 40% the plasma concentrations of vitamins C and E. The lipid peroxidation product malondialdehyde tended to be lower in pulmonary lavage fluid following antioxidant supplementation compared to placebo and control periods. The moderate intensity exercise test did not induce an adequate oxidative stress response to detect effects of exercise or supplementation. It was concluded that antioxidant supplementation has no effect in healthy horses fed adequate diets. While there are other products intended for equine use that have antioxidant potential (Cecchini *et al*. 2014)), there is little research at this time examining effects on inflammation, oxidative stress and immune health.

Vitamin E is a commonly supplemented antioxidant in horses despite the fact that when horses were supplemented with vitamin E, a single bout of submaximal exercise had no effect on plasma vitamin E status (Siciliano *et al*. 1997). In contrast, when horses were supplemented with vitamin E at 5000 IU / day (5 times the NRC recommendation) plasma creatine kinase was less, and plasma concentrations of a-tocopherol, total glutathione and glutathione peroxidase were less, than controls during endurance exercise (Williams *et al*. 2004). In a subsequent study, Williams and Carlucci (2006) supplemented 3 levels of vitamin E (0, 5000 or 10,000 IU / day) above a basal level of 120 IU /day to unfit Standardbred horses that were subjected to periods of high intensity exercise. The high intensity interval exercise test consistently increased plasma α-tocopherol, retinol, beta-carotene and erythrocyte total glutathione and glutathione peroxidase with exercise, with no effect of Vitamin E treatment. It was concluded that when horses were supplemented with even high amounts of vitamin E (~10-times the 1989 NRC recommendation) there was no attenuation of the oxidative stress associated with high intensity exercise.

To try to improve bioavailablity of vitamin E, Rey *et al*. (2013) administered a micellized natural vitamin E (1,400 IU / day) at 12 h and 1 h before training to 10 Thoroughbred racehorses in training. The supplement was given orally for 1 day or for 8 days. Plasma antioxidant status (α-tocopherol, thiobarbithuric acid-reactive substances (TBARS), total glutathione, and trolox equivalent antioxidant capacity (TEAC) were assessed from blood samples taken immediately before exercise training, after intense training and after 8 h of recovery. Supplementation did not affect glutathione but significantly increased α-tocopherol and TEAC, particularly after 8 days. Exercise resulted in an increase in TBARS in all treatments, and the lowest TBARS occurred at 8 h of recovery after horses were supplemented for 8 days. The control group was not able to maintain TEAC after intense exercise indicating inadequate antioxidant supply / activity to combat the exercise-induced oxidative stress. The authors concluded that micellized natural vitamin E improved the horses' ability to maintain oxidative status during and after high intensity exercise training.

In comparison to vitamin E supplementation alone, 70 days of supplementation of vitamin E (40 mg / kg of feed) with selenium (20 mg/kg of food) increased erythrocyte resistance to the peroxidative stress and lymphocyte glutathione peroxidase activity in vitro (Avelinni *et al*. 1999). Plasma markers of cell membrane lipid peroxidation (malondialdehyde) and markers of antioxidant status increased. The authors concluded that the combination of exercise training, selenium and vitamin E supplementation were effective in increasing antioxidant defences and decreasing peroxidative damage following physical exercise.

The equine literature on Vitamin E supplementation has commonality with the literature on other mammals, with heterogeneity with respect to exercise designs and outcome measures. In order to address this feature, and the resulting contractions in opinions, Stepanyan *et al*. (2014) performed a meta-analysis of

20 relevant studies, of which 6 were highly relevant. From these data, the authors concluded that Vitamin E supplementation was without significant protective effect against exercise-induced muscle damage or membrane lipid peroxidation.

N-acetylcysteine

Human studies have used a different approach to attenuate the muscle damage associated with intense exercise. N-acetylcysteine is a thiol-based antioxidant capable of attenuating the respiratory burst and MAPK- and NF-kB–mediated pro-inflammatory cytokine release in response to the initial muscle inflammation (Aoi *et al*. 2004). Because of this characteristic response is may be undesirable to use NAC when one is trying to achieve beneficial muscle adaptations, i.e. training effects (Petersen *et al*. 2012).

Michailidis *et al*. (2013) administered a single dose of NAC (20 mg / kg body mass / day) as a potent antioxidant immediately after severe exercise stress (300 eccentric contractions of the vastus lateralis) and assessed the response of skeletal muscle inflammatory markers and redox-sensitive signalling during the initially inflammatory and subsequent repair phases. Compared to placebo, NAC was effective in blunting 1) the rise in inflammatory markers of muscle damage (creatine kinase activity, C-reactive protein, proinflammatory cytokines, nuclear factor κB phosphorylation); 2) redox-sensitive signalling (decreased phosphorylation of protein kinase B, mammalian target of rapamycin, p70 ribosomal S6 kinase, ribosomal protein S6, and mitogen activated protein kinase p38); and 3) the decrease in strength during the first 2 d of recovery. The attenuation of the signalling responses persisted through 8 days of recovery. Interestingly, NAC treatment prevented functional recovery, such that muscle performance fully recovered only in the placebo group.

Creatine and antioxidant status

Creatine is an often-used, nonessential dietary supplement that is used to increase the pool of metabolically active creatine within muscle, with the aim of increasing muscle strength and performance (Jager *et al* 2011). Creatine endogenously synthesized in the liver travels in the blood and is taken up by muscle and other cells. An increase in the content of muscle phosphocreatine, the high energy ATP buffer, aids in the provision of ATP during short-term, high intensity exercise. In contrast to numerous human studies (reviewed by Schoch *et al*. 2006; Jager *et al*. 2011), creatine supplementation in horses was without effect on muscle metabolic responses (Schuback *et al*. 2000). The absence of response may be attributable to the low dose (25 g twice daily) and brief 6.5-day duration of supplementation.

That creatine acts as an antioxidant, scavenging ROS, was initially shown by Lawler (2002). Creatine protects against oxidative stress in cultured cells, reduces DNA and RNA damage, and anti-inflammatory activity in living rats (see Sestili *et al*. 2011). In addition to these effects creatine, when supplemented to cultured cells, reduced the RNA-damaging activity of H_2O_2 indicating a capacity to directly scavenge free radicals and/or to maintain the cellular pool of high energy phosphates (Fimognari *et al*. 2009). Bassit *et al*. (2008) and Deminice *et al*. (2013) have shown that creatine supplementation (0.3 g / kg body weight) attenuated the rise in inflammatory markers induced by strenuous exercise in humans. However this is not associated with similar effects on plasma markers of oxidative stress (Deminice *et al*. 2013). In contrast, creatine supplementation (0.3 g / kg) in rats for 2 weeks before 1 hour of eccentric to exhaustion was without effects on skeletal muscle markers of inflammation and oxidative stress (Silva *et al*. 2013).

Conclusions on the supplementation of antioxidants

The best evidence that supplemented antioxidants are beneficial comes from in vitro cell systems. However there has been difficulty in translating such results into living organsims, and specifically with horses experiencing metabolic stress due to exercise. In vivo systems frequently generate extensive modification of products intended for target tissues to unknown compounds that may or may not exert beneficial effects that are seen in vitro. There remains a strong need to look at ways of inducing endogenous anti-oxidant systems – sometimes this occurs by supplementation with a similar compound, the case of exogenously supplied SOD for example. In contrast, dietary supplementation with vitamin E does not appear to be useful. Additional research using creatine, because of its potential for ROS scavenging and elevation of cellular high energy balance. Hundreds of formulations on the market touted as immune enhancing, anti-inflammatory and antioxidant, but there is very little evidence to support such claims in living animals. And there remains the concern that too strong an anti-oxidant or anti-inflammatory effect will hinder the muscle's / body's ability to adapt in a positive way to the stresses.

Supplements for immune support

Because of the interplay between oxidative stress, inflammation and immune function, researchers are interested in approaches to enhance immune function. Enhanced functions of the immune system would be manifest in improved defense against oxidative stress and stress-induced inflammation.

Omega-3 fatty acids

Omega-3 fatty acids, most often from flaxseed and fish oil, are increasingly supplemented to the diet because of wide-ranging anti-inflammatory and immune enhancing properties in humans and other mammals (Calder and Grimble, 2002). Supplementation with omega-3 oils 'positively' affects blood and muscle fatty acid composition in horses (Vineyard *et al*. 2010; Hess *et al*. 2012) and may show enhancement of some immune parameters (Vineyard *et al*. 2010). There are no data in horses examining a potential ergogenic, immune enhancing or anti-inflammatory benefit. However, a recent review of the human literature concluded that at present there is inadequate evidence to show that omega-3 fatty acids are ergogenic, or effectively attenuate the inflammatory and immunomodulatory responses to exercise (Shei *et al*. 2014).

Beta-glucans

Beta-glucans are a class of polysaccharides derived from cell walls of yeast, fungi, algae, and oats. Horses consuming out and oat products as a normal part of their diet will be receiving oat beta-glucans. There are numerous supplements on the market touting the benefits of beta-glucan for horses, however there has been no research to date showing a benefit that can be directly attributed to supplemented beta-glucans. Beta-glucans in general, when supplemented to the diet, enhance immune system functions via direct stimulation of macrophages, neutrophil, and NK cells (Vetivicka *et al*. 1996). As a result, beta-glucan supplementation has been associated with improved defense against microbial challenges in vitro and in vivo (Estrada *et al*. 1997; Brown *et al*. 2001; Davis *et al*. 2004).

Work from the Davis lab also showed that oat beta-glucan increased both neutrophil number and neutrophil respiratory burst activity in mice performing volitional, moderate intensity though exhaustive exercise over a 6-day period designed to mimic weekly training efforts (Murphy *et al*. 2007). Moderate intensity exercise also increased neutrophil respiratory burst activity, while three days of high intensity exercise did not. McFarlin *et al*. (2013) applied this approach of combatting post-exercise immune suppression to 182 men and women who had competed in a marathon. Participants received either yeast beta-glucan or placebo. Amongst participants receiving beta-glucan there was a 37% reduction in cold / flu symptoms compared to placebo. This group also studied the effects of yeast beta-glucan supplementation on the post-exercise concentrations of pro-inflammatory monocytes and cytokines (Carpenter *et al*. 2013). The concentrations of the plasma cytokines IL-4, IL-5 and IFN-γ were greater following beta-glucan supplementation compared to placebo, and this was associated with increased monocyte cytokine production in vitro. The authors concluded that beta-glucans have the potential to alter immune function after strenuous exercise. Results consistent with these have been shown in elite athletes during periods of strenuous training (Bobovčák *et al*. 2010).

An additional benefit of beta-glucan supplementation may occur by downregulating the expression of stress-induced fatigue indicators (c-Fos and c-Jun) in the central nervous system, as shown in the brain of rats exercised to exhaustion (Hong *et al*. 2014). This result is consistent with an increased exercise duration compared, to controls, in rats receiving long-term (7 weeks) dietary supplementation of oat beta-glucan and trained to perform prolonged exercise (Xu *et al*. 2013).

In conclusion, there is evidence that beta-glucan supplementation may be beneficial in human exercise performance, however there is no evidence at this time that this may also be the case in horses.

Summary

The present research provides tantalizing indications of the potential for benefit from such supplements. The heterogeneity with respect to supplement dosage and duration, timing of tissue sampling for outcome measures, and paucity of positive outcomes likely means that horses were under-supplemented in some studies, and that peak effects may have been missed in other studies. Definitive research, using well-designed studies with well-defined outcome measures are still needed in order to allow us to come to some firm conclusions regarding the touted benefits of supplements having anti-oxidative and anti-inflammatory potential.

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