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Review

Some commonly fed herbs and other functional foods in equine nutrition: A review

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Abstract

Most herbs and functional foods have not been scientifically tested; this is especially true for the horse. This paper reviews some of the literature pertinent to herbal supplementation in horses and other species. Common supplements like Echinacea, garlic, ginger, ginseng, and yucca are not regulated, and few studies have investigated safe, efficacious doses. Ginseng has been found to exert an inhibitory effect on pro-inflammatory cytokines and cyclooxygenase-2 expression. Equine studies have tested the anti-inflammatory effects of a single dose of ginger, post-exercise. Echinacea has been reported to have anti-inflammatory and antioxidant properties. Yucca contains steroid-like saponins, which produce anti-inflammatory, antioxidant, and anti-spasmodic effects. However, some herbs have drug-like actions that interact with dietary components and may contain prohibited substances like salicylates, digitalis, heroin, cocaine and marijuana. Horses fed garlic at >0.2 g/kg per day developed Heinz body anaemia. Drug–herb interactions are common and caution needs to be taken when implementing ‘natural product’ usage.

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Introduction

Herbal medicine, also called “phytomedicine”, is the use of therapeutic plants, plant parts or plant derived substances to aid in fighting against infections, diseases or enhancing overall health (Jonas, 1997). In 1999, the world market for botanicals and homeopathies was US\$¹19.4 billion, with Europe in the lead with \$6.7 billion, followed by Asia (\$5.1 billion), North America (\$4.0 billion), Japan (\$2.2 billion), and the rest of the world (\$1.4 billion) (Laird and Pierce, 2002). In the European market alone, Germany had the highest annual sales (\$3.5 billion US\$), with France (\$1.8 billion) and Italy (\$700 million) following (Anon, 1999).

One study specifically focused on the United States reported that the herbal market exceeds \$3.2 billion in sales, where 32–37% of Americans use herbal agents each year (Johnston, 1997). In more recent years, the United States herbal market value was thought to be higher than in previous years, with garlic and Echinacea being the top two selling herbs, respectively (Blumenthal, 2005). The horse industry in the United States was surveyed in 1997 regarding supplement use and it was found that about 70% of horse owners or other stakeholders fed one type of supplement or another. Furthermore, nearly 5% of those operations fed herbal supplements (United States Department of Agriculture, 1998). Since then, it is thought that the herbal market targeting horses has grown exponentially; however no new statistical data are available on the subject.

Herbal supplements that affect the immune system can be classified as adaptogens, immunostimulants or both.

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¹ US\$1 = approx.£0.50; €0.72.

Adaptogens increase resistance to stressors, physical, chemical or biological, where immunostimulants activate the nonspecific, or innate defense mechanisms against viral, bacterial or cellular infections. Most of the studies to date in laboratory animals, humans and other species have determined that the immunological effects of herbal supplements does not enhance healthy immune function but may help if the immune system is compromised (Parnham, 1996; Schulz et al., 1998).

This review will focus on specific herbs and other functional foods that are commonly used in the horse industry. Published literature, however, is scarce so research from humans and other species has been included to better illustrate the actions of the supplements.

Actions and uses

Table 1 summarizes the active component, action, drug interactions, and equine research present for the major herbs and other functional foods described.

Bee pollen and propolis

Bee pollen and propolis are similar resinous substances collected from various plant sources by honeybees. Propolis has been proven to contain polyphenols, and flavonoids, as well as several specific antioxidant compounds including β -carotene, caffeic acid, kaempferol, phenethyl caffeate, *p*-hydroxyacetophenone, benzylhydroxybenzoate, coumaric

Table 1
Herbal supplements and other functional foods

Common name	Scientific name	Active components ^a	Actions ^a	Potential toxicity or interaction ^b	Equine research
Bee pollen	Propolis	β -Carotene, caffeic acid, kaempferol, phenethyl caffeate, <i>p</i> -hydroxyacetophenone, benzylhydroxybenzoate, coumaric, cinnamic acid	Antioxidant, antimicrobial, antifungal, anti-inflammatory, immunoregulatory	None reported	Turner et al., 2006
Devil's claw	<i>Harpagophytum procumbens</i>	Iridoid glycosides, acetylated phenolic glycosides, terpenoids	Anti-inflammatory	Cause gastric ulcers, prolong bleeding time	Pearson et al., 1999
Echinacea	<i>Echinacea purpurea</i> , <i>E. angustifolia</i> , <i>E. pallida</i>	Polysaccharides, glycoproteins, alkamides, cichoric acid	Anti-inflammatory, antioxidant	May interfere with drugs processed by liver enzymes, not for use with a depleted immune system, or during pregnancy, possible allergic reactions	O'Neill et al., 2002b
Flaxseed	<i>Linum usitatissimum</i>	ω -3 Fatty acids, phytoestrogens, flavonoids	Antioxidant, anti-inflammatory, chemopreventive	May decrease or prolong absorption of other drugs, prolong bleeding time	O'Neill et al., 2002a; Hansen et al., 2002
Garlic	<i>Allium sativum</i>	Sulfoxides, gamma-glutamylcysteines	Anti-bacterial, anti-viral, anti-fungal, anti-parasitic	Heinz body anemia, uterine stimulant, prolong bleeding time, gastric ulcers	Pearson, 2003; Pearson et al., 2005
Ginger	<i>Zingiber officinale</i>	Paradol, gingerol, myoga	Anti-inflammatory, anti-thrombotic, antioxidant, anti-bacterial	Cause gastric ulcers, prolong bleeding time	Liburt, 2005
Ginseng	<i>Panax ginseng</i> , <i>Panax quinquefolius</i> , <i>Eleutherococcus senticosus</i>	Ginsenosides, essential oils, phytosterols	Anti-inflammatory, antioxidant	May interfere with drugs processed by liver enzymes, potentiate diuretics, decrease blood sugar, decrease coagulation	N ^c
Valerian	<i>Valeriana fauriei</i> , <i>V. officinalis</i> , <i>V. edulis</i> , <i>V. wallichii</i>	Valerenic acid, iridoid glycosides	Sedative, anti-spasmodic	May enhance effect of tranquilizers and anesthetics, may be prohibited substance, cause diarrhea and colic	N
Yucca	<i>Yucca schidigera</i>	Saponins, resveratrol, yuccaols A-E	Anti-inflammatory, antioxidant, anti-spasmodic, anti-platelet	May accelerate NSAID's, cause diarrhea	N

^a For references regarding ingredients or actions see text for the specific herb.

^b Information compiled from Miller (1998), Poppenga (2001), Harman (2002) and Izzo et al. (2005).

^c N= no reference available.

and cinnamic acid (Ahn et al., 2004; Gomez-Caravaca et al., 2006; Christov et al., 2006). The composition of propolis varies greatly as a result of collection from different geographic regions, the time of collection, and various species of vegetation from which the pollen is collected. Reported biological properties include antioxidant, antimicrobial, antifungal, anti-inflammatory, and immunoregulatory actions (Liebelt and Calcagnetti, 1999).

Propolis with strong antioxidant activity, as determined by β -carotene bleaching, 1,1-diphenyl-2-picrylhydrazyl free radical scavenging, and 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) radical cation decolorization assays, was also found to have high total polyphenol content (Ahn et al., 2004). Additionally, propolis and polyphenolic compounds derived from propolis were found to have immunomodulatory effects evidenced by decreased pulmonary tumor nodules in mice with experimentally transplanted tumors (Orsolich et al., 2004). Tichy and Novak (2000) found a mixture of antimicrobial compounds in ethanol extracts of propolis that were effective in inhibiting *viridans Streptococci*. Furthermore, several different propolis samples were found to exhibit significant antimicrobial activity against Gram-positive bacteria and yeasts (Uzel et al., 2005).

Anti-inflammatory effects of propolis were found in a mouse paw edema model in which nitric oxide (NO) inhibition occurred after propolis administration (Tan-No et al., 2006). Ethanol and water extracts of propolis were effective in reducing inflammation purportedly through the inhibition of prostaglandin (PG) E₂ and NO levels in ICR and Wistar rats with induced edema, pleurisy, and acute lung damage. Additionally, these same rats with induced arthritis exhibited reduced interleukin (IL)-6 in inflamed tissues after administration of propolis extracts (Hu et al., 2005). These results indicate a whole host of beneficial effects of propolis in various species, with few adverse allergic reactions found in some human clinical cases; however, care should be taken if supplementing to horses as similar effects might occur.

Little research has been done to evaluate the efficacy of bee pollen or propolis supplements in horses so the validation of bee pollen used in other species as an anti-inflammatory product has yet to be determined. There are however numerous anecdotal reports of the benefits of supplemented bee pollen in horses including improved oxygen utilization, lower heart rates and firmer muscle tone (Turner et al., 2006). A recent pilot study in horses examined the effects of bee pollen based supplementation on physical fitness parameters, immunological status and nutritional variables in ten Arabian horses in training. Results indicated that supplementation with 118 g of a commercial 55% bee pollen supplement for 42 days did not alter physical fitness or immunological variables in the horses. However, supplementation did significantly increase feed intake and subsequently increased the nutrient retention of nitrogen and phosphorus in the same horses (Turner et al., 2006). The authors of the study the-

orized that the increased feed intake in these horse resulted from the high content of B vitamins, particularly thiamin which is used as a cofactor in energy metabolism. Similar results were seen in rats supplemented with propolis which showed increased weight gain, improved utilization of iron, increased calcium and phosphorus absorption, and improved regeneration efficiency of hemoglobin (Haro et al., 2000). These results could prove valuable when trying to produce weight gain in horses or in horses with poor nutrient digestibility.

Devil's claw

Devil's claw (*Harpagophytum procumbens*) is reported to have an anti-inflammatory effect in humans and laboratory animals. On the animal health market, devil's claw is primarily sold for its pain killing and anti-inflammatory properties, and there are many testimonials claiming relief from rheumatism and other joint disorders (Anon, 2003). Its effectiveness could be dependent upon the route of administration and may not be effective in the form of an intraperitoneal injection. The active ingredients are various iridoid glycosides, acetylated phenolic glycosides, and terpenoids. Multiple studies, which are reviewed in Chrubasik et al. (2002), have shown that extracts with >50 mg of harpagoside (a glycoside) per day are helpful in alleviating lower back pain in humans. Most of the human clinical studies reported a decrease in pain intensity and an increase in flexibility after being supplemented with devil's claw extract. These results could potentially be transferred to equine medicine when dealing with flexibility or potential clinical efficacy (i.e. flexion tests); however, the authors are unaware of any exclusive devil's claw studies performed in horses.

One study in laboratory animals has shown that topical application of devil's claw decreases the expression of cyclooxygenase (COX)-2, which is a rate-limiting enzyme involved in the inflammatory cascade (Kundu et al., 2005). However, it was not clear in this study as to which specific active ingredients were contributing to this action. Harpagoside alone has been shown to suppress COX-2 and inducible nitric oxide synthase (iNOS) at both the mRNA and protein level in vitro (Huang et al., 2006). However, it did not exhibit any inhibitory effect on COX-1 activity, so the activity of harpagoside was not attributed to the antioxidant properties of devil's claw. Its effectiveness in reducing pain and inflammation associated with rheumatoid and osteoarthritis can be explained by its ability to block the production of inflammatory mediators such as PGE₂ (Chantre et al., 2000). A more recent report in rabbits indicated that there was a chondroprotective effect of devil's claw shown by an increase of metalloproteinase-2 in treated animals (Chrubasik et al., 2006).

A blinded, placebo controlled, cross-over designed study in horses with naturally occurring osteoarthritis looked at the effect(s) of a proprietary polyherbal composite joint supplement containing devil's claw. An anti-inflammatory

effect was observed in the horses due to a reduction in PGE₂ synovial fluid content (Pearson et al., 1999). However, all but one of the six horses used in this study had no change in lameness or flexion score when tested by a veterinarian.

A few negative impacts of devil's claw have been shown by the potential to cause gastrointestinal upset linked to gastric ulcers (Izzo et al., 2005). However, other drug interactions in various species have not been reported (Harman, 2002) and no evidence of interactions has been reported in horses.

Echinacea

Echinacea (*Echinacea* spp.), a common immunostimulant, or 'cold fighter', has been reported to have anti-inflammatory and antioxidant properties. The equine industry typically uses Echinacea as an immune booster to compliment a healthy immune system (Anon, 2003). It is recommended that the best way to use Echinacea is to supplement at the first signs of illness or infection. If administered too late in the cycle the herb will be less effective.

In humans (Wagner and Jurcic, 1991) and mice (Roesler et al., 1991), Echinacea extracts have been proven to stimulate phagocytosis. Other studies have demonstrated a stimulatory effect on lymphocyte function and proliferation in normal and diseased human mononuclear cells in vitro (See et al., 1997).

Three main species include *Echinacea purpurea*, *Echinacea angustifolia* and *Echinacea pallida*. These species have been studied for their medicinal properties and were found to have a wide range of benefits (Block and Mead, 2003). Many research studies have looked at the biochemistry, immunopharmacology and clinical use of Echinacea (Bauer et al., 1988; Wagner and Jurcic, 1991; Wildfeuer and Mayerhofer, 1994; Parnham, 1996; Gunning and Steele, 1999). The common active components of these various Echinacea species include polysaccharides, glycoproteins, alkaloids, and cichoric acid, which is a derivative of caffeic acid. However, it must be noted that depending on the species and commercial preparation of these products, the concentrations of these components will vary greatly. Some human studies have found that Echinacea can enhance cytokine production, including tumor necrosis factor α (TNF- α), IL-1, IL-6 and IL-10, by macrophages (Burger et al., 1997).

Echinacea has been used in some 30 randomized, controlled trials and there were no adverse effects in regards to overdoses or drug interactions (for review see Barrett, 2003). However, there have been reports of allergic reactions (Biology, 2002) and anaphylaxis (Mullins, 1998; Mullins and Heddle, 2002) associated with Echinacea supplementation in humans. Parnham (1996) has also reviewed the safety of Echinacea, and in his report has detailed several reports of adverse effects with allergic reactions to Echinacea products.

One placebo-controlled, randomized study used eight horses that were supplemented with Echinacea for 42 days at a level equivalent to 1000 mg standardized extract (O'Neill et al., 2002b). They concluded that the horses treated with Echinacea were immune stimulated, although the results only showed increases in lymphocyte count and decreases in neutrophil count at day 35 of the 42 day supplementation period. Increases in red blood cell count and hemoglobin were also found over time.

Flaxseed

Flaxseed (*Linum usitatissimum*) contains high levels of ω -3 fatty acids, which is a good source of α -linolenic acid, phytoestrogens, flavonoids, and various amino acids and minerals (Cunnane et al., 1993). It is marketed for its high ω -3 fatty acid content and is used in coat, skin, and hoof conditioners for horses and is often marketed to enhance hair coat quality. Due to its soluble fiber content comparable to that of oat bran, flaxseed is used most often in humans as a laxative. Flaxseed has also been evaluated for potential anti-inflammatory properties as a potential preventative or treatment for inflammatory diseases or conditions. Recently there have been an increased number of equine supplements containing flaxseed or linseed components, but published research is limited.

Recently the role of ω -3 fatty acids has received considerable attention. One study found that six exercising horses supplemented for 4 weeks with an oral antioxidant supplement enriched with ω -3 fatty acids (α -tocopherol, eicosapentaenoic acid and docosahexaenoic acid) induced changes in membrane composition; therefore a significant decrease in erythrocyte membrane fluidity was not seen during exercise when compared to placebo-treated horses (Portier et al., 2006). Another study evaluated exercising horses that had been supplemented with 324 mg/kg body-weight (BW) fish oil containing 10.6% eicosapentaenoic acid and 8% docosahexaenoic acid or corn oil for 63 days during which time they were exercised five times per week culminating with a stepwise treadmill exercise test (O'Connor et al., 2004). When compared to corn oil, the fish oil supplemented horses exhibited lower heart rates and tended to have lower hematocrits, along with a lower serum insulin concentration, although the glucose:insulin ratios were higher.

Further studies in horses have evaluated supplementation effects of essential free fatty acids (FFA). Henry et al. (1991) found that in endotoxin challenged horses, an 8 week supplementation of an 8% linseed oil ration containing α -linolenic acid resulted in longer mean whole blood recalcification time and activated partial thromboplastin time when compared to horses fed a control ration. Neelley and Herthel (1997) found that horses supplemented daily with two cups of an essential FFA supplement for a minimum of 1 month did not develop laminitis after receiving a laminitis ration of carbohydrates via nasogastric tube when compared to non-supplemented

horses. In another study, horses suffering from recurrent airway obstruction were supplemented with equivalent amounts (320 mg/kg BW/day) of sunflower oil (linoleic acid) or seal blubber oil (70–75 mg/kg BW long chain $n-3$ polyunsaturated fatty acids [$n-3$ PUFAs]) for 10 weeks (Khol-Parisini et al., 2007). The fatty acids were found to be incorporated into leukocyte cell membranes overall. Additionally, there was a reduction in $n-6:n-3$ ratios in plasma and leukocyte phospholipids, and pulmonary epithelial lining fluid leukocyte counts with the seal blubber oil treatment vs. the sunflower oil treatment. In a separate study it was determined that 18 weeks of supplementation with a 10% flaxseed oil to six horses did not significantly change their bodyweight, complete blood count, plasma fibrinogen, electrolyte (Na, K, Cl) concentrations, and biochemical profile of enzyme activities when compared to control horses (Hansen et al., 2002).

Other studies have investigated the role of flaxseed supplementation on hair and skin coat quality. One study tested flaxseed as a treatment for allergic skin diseases in horses and found a significant improvement in a skin test response to *Culicoides* spp. or 'sweet itch' when compared to placebo treated horses (O'Neill et al., 2002a). Rees et al. (2001) found that after supplementing flaxseed to 18 dogs for at least 1 month, the relative percent of 18:3 $n-3$ and 18:2 $n-6$ concentrations in serum phospholipids increased followed by improved hair coat and skin condition scores compared to pre-supplement.

Research studies in other species have reported antioxidant, anti-inflammatory, and chemopreventive properties of flaxseed and flaxseed oil. One study reported that in male Fischer rats with experimentally-induced carcinogenesis of the gastrointestinal tract, 15% flaxseed diet supplementation significantly increased colon tissue and serum levels of $\omega-3$ fatty acids, decreased size and incidence of tumors, as well as decreased COX-1 and -2 levels (Bommareddy et al., 2006). Another study evaluated the antioxidant properties of flaxseed supplementation in albino rats challenged with carbon tetrachloride (CCl₄) toxin. Results indicated a 1.2-fold increase in the lipid peroxidation value, increased restoration of catalase, superoxide dismutase, and peroxidase compared to CCl₄ challenged control animals (Rajesh et al., 2006). Additionally, work was done to evaluate nutrient utilization in dairy cows following flaxseed supplementation and found that total tract nutrient utilization was improved without adverse effects on ruminal fermentation (Gonthier et al., 2004).

There is some concern about the possibility of cyanide poisoning in horses fed flaxseed, which is why it is commonly boiled to remove the potentially toxic cyanide components (Oomah et al., 1992). However, symptoms do not become evident for a long time and no reported symptoms were evident in the study by O'Neill et al., (2002a,b). In theory, the lack of toxicity was attributed to the ability of the stomach acid to inactivate enzymes within the seeds, which are required to interact with the glycosides to form cyanide. Further research is needed to determine if horses

on anti-ulcer supplements or medication would be at greater risk of cyanide poisoning.

Garlic

Garlic (*Allium sativum*) has a broad anti-microbial spectrum, and anti-parasitic properties. Garlic's active components include organosulfur compounds, which are responsible for the majority of garlic's physiological effects. The intact bulb of the garlic plant contains a complex mixture of cysteine sulfoxides, and γ -glutamylcysteines. When the bulb is disrupted the sulfoxidases are cleaved to the active form of thiosulfinate allicin (Munday and Munday, 2001). Garlic is typically included in equine supplements for its expectorant action to help break up mucous. However, this action is secondary to the primary use of garlic in the horse industry as an insect repellent. A study conducted by Valerio and Maroli (2005), evaluated the repellent effect of garlic oil applied topically on human volunteers exposed to female sandflies and found that a 1% and a 0.005% garlic oil dilution provided 97% and 40% repellent effectiveness, respectively.

Garlic has been shown to have a wide range of anti-parasitic properties that are effective against at least 12 human and non-human parasites (Anthony et al., 2005). Components within garlic oil including, allicin, diallyl trisulphide (DAT, – a transformation product of allicin), and ajoene are effective against a variety of trophozoite, protozoan, plasmodium, trypanosome, coccidian, and flagellate species. The mode of action of garlic oil varies depending on the parasitic species and can include inhibition of macrophage NO production, interaction with thiol-containing enzymes, inhibition of cysteine proteinases, alcohol dehydrogenases, and thioredoxin reductases, inhibition of phosphatidylcholine biosynthesis, interference with protein and lipid trafficking in parasite and host cell membranes, alteration of intracellular membranous structures, inhibition of parasitic synthesis of coenzyme Q and cell lysis (for review see Anthony et al., 2005).

Crushed garlic preparations have been shown to have antibacterial properties. Certain strains of Gram negative and Gram positive bacteria have exhibited sensitivity to allicin (for review see Ankri and Mirelman, 1999; Chowdhury et al., 1991). A preliminary study by De et al. (1999) screened 35 different Indian spices for antimicrobial activity and found that an aqueous solution of *Allium sativum* at 100 mg/mL was effective in inhibiting the growth of *Bacillus subtilis*, a Gram positive bacteria in vitro. Another study found that a 57.1% w/v aqueous garlic extract containing 220 μ g/mL allicin was effective in inhibiting the growth and killing several oral microorganisms including periodontal pathogens maintained on various agars supplemented with horse blood (Bakri and Coughlas, 2005). Additionally, certain viruses including human cytomegalovirus, influenza B, herpes simplex virus type 1 and 2, parainfluenza virus type 3, vaccinia virus, vesicular stomatitis virus and human rhinovirus type 2, as well as some fungi have

shown sensitivity to fresh garlic extracts in which ajoene and allicin are thought to be the active components (Ankri and Mirelman, 1999).

The high sulfur content of garlic is theorized to help cleanse the blood (Anon, 2003). In one study, the efficacy of 'Breath', a polyherbal composite supplement containing garlic, was evaluated in horses with naturally occurring, symptomatic chronic obstructive pulmonary disease (COPD). A significant decrease in respiratory rate was found with no deleterious effects detected in hematology and biochemistry screenings (Pearson, 2003).

Garlic extracts containing phytochemicals have been shown to have antioxidant properties in other species. The antioxidant characteristics of garlic extract manifest themselves in reactive oxygen species (ROS) scavenging, and enhancing cellular antioxidant enzyme status including superoxide dismutase, catalase and glutathione peroxidase. Garlic extract is further attributed to inhibiting lipid peroxidation, protecting DNA against free radical-mediated damage and mutations, inhibiting multi-step carcinogenesis, protecting against some forms of ultraviolet-induced immunosuppression, and preventing age related deterioration of brain function (in a senescence-accelerated mouse model) (Borek, 2001; Thabrew et al., 2000). In one study lipid peroxidation, and *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine (MNNG)-induced bone marrow nuclei were reduced in male Swiss mice pre-treated with an aqueous extract of garlic (3.75 mg/mL at 125 mg/kg BW) vs. those pre-treated with water for 5 days (Kumaraguruparan et al., 2005). A similar study found higher concentrations of antioxidants and detoxifying stomach enzymes and reduced circulating and hepatic lipid peroxides in rats supplemented with garlic extract vs. the control rats (Arivazhagan et al., 2000). Another study in rats found an increased resistance to lipid peroxidation in liver, lung and heart tissues when induced by nicotine, along with a increased activity of antioxidant enzymes, and increased concentrations of glutathione when supplemented with garlic and onion oils for 21 days at a concentration of 100 mg/kg bodyweight compared to controls (Helen et al., 1999).

Toxicity is a possibility with symptoms including gastric irritation, decreased sperm production, Heinz body anemia, and occupational asthma. In dogs, 5 g/kg of fresh garlic increased oxidation of hemoglobin within red blood cells and decreased total hemoglobin concentration (Hu et al., 2002). Garlic consumption also led to oxidation of red blood cells in sheep (Stevens, 1984). Equine studies found that freeze dried garlic fed at >0.4 g/kg per day resulted in symptoms indicative of Heinz body anaemia (Pearson et al., 2005). In this study 100% of the horses ($n = 2$) fed garlic showed an increase in mean corpuscular volume, Heinz body score, platelet count, serum-free and total bilirubin concentration, and decreases in red blood cell count, blood and mean corpuscular hemoglobin concentration, and serum haptoglobin concentration. The existing evidence of antimicrobial, anti-parasitic, antioxidant, and insect repellent properties of garlic preparations

in vitro and in other species warrants further research to establish dose response and efficacy of this herb in equines.

Ginger

Ginger (*Zingiber officinale*) has been shown to have anti-thrombotic, antioxidant, anti-inflammatory, and anti-bacterial properties. In the 1970s ginger was first found to have anti-inflammatory properties including inhibition of prostaglandin synthesis (Kiuchi et al., 1982). After that time more research was completed and it was found that major constituents in ginger include paradol, gingerol, and myoga (for review, see Grzanna et al., 2005).

[8]-Paradol, a natural constituent of ginger, has shown anti-inflammatory properties as a potent COX-1 inhibitor and anti-platelet aggregation in human whole blood. These properties make it a potential treatment for musculoskeletal disorders (Srivastava and Mustafa, 1992). Ginger has shown potential for use in cancer treatment. 6-Gingerol, another natural constituent of ginger, protected human leukemic HL60 cells from oxidative stress and induced cell death in promyelocytic leukemia HL60 cells. It also caused DNA fragmentation and inhibited Bcl-2 expression. Another component of ginger, myoga (*Zingiber mioga* Roscoe), showed powerful cytotoxic effects on human T lymphoma Jurkat cells. Recently ginger has received attention due to anti-inflammatory properties extending beyond the inhibition of prostaglandins (Grzanna et al., 2005).

A recent cross-over design study on nine horses tested a single dose of ginger on anti-inflammatory and cardiovascular effects post-exercise (Liburt, 2005). Intensely exercised horses, until the point of fatigue, given ginger extract 1 hour prior to exercise had a reduced recovery time in the fast phase of the VO₂ recovery curve where the metabolic cost of exercise is rapidly replenished. On the other hand, ginger has a tendency to increase pro-inflammatory cytokines TNF- α and interferon (IFN)- γ . It was speculated that the caustic ginger extract solution irritated the gastrointestinal tract after ingestion, which could be confounded by the increased creatine kinase levels seen after this administration as well (Liburt, 2005). Even though ginger has been theorized in horses and proven in humans to cause gastric ulcers (Izzo et al., 2005), many ulcer relief herbal supplements for horses contain ginger as a major ingredient.

Ginseng

Ginseng (*Panax* spp.) is commonly studied in terms of its immunostimulatory properties. It has been found to exert an inhibitory effect on IL-1 β and IL-6 gene expression, to decrease TNF- α production by macrophages, decrease COX-2 expression, and suppress histamine and leukotriene release (for review, see Radad et al., 2006). On the equine supplement market, ginseng is marketed and sold for use in stimulating the immune system, decreas-

ing stress, and increasing optimal performance, however no published research has been found at this time.

Ginseng has three main species of interest: the Asian ginseng is *Panax ginseng*, the American ginseng is *Panax quinquefolius*, and the Siberian ginseng is correctly called “eleuthero” or *Eleutherococcus senticosus* (for review see Block and Mead, 2003). The main component of each species includes glycosidal saponins called ginsenosides. Other minor components include essential oils, phytosterols, amino acids, peptides, vitamins and minerals. Many of the ginsenosides have antioxidant properties that protect membranes of nerve and immune cells.

Studies using human immune cells have demonstrated a stimulating effect on lymphocyte function and proliferation in vitro in normal and diseased human mononuclear cells (See et al., 1997). The results from this study are consistent with other published research on its immune-stimulating properties in laboratory animals and humans. The authors theorize that the results found with ginseng in other species could also potentially be adapted for horses, although without the equine specific studies no definitive conclusions can be made. One should be careful when using ginseng in horses that are under long term use of non-steroidal anti-inflammatory drugs (NSAIDS) as these have the potential to interact with each other (Miller, 1998; Poppenga, 2001).

Valerian

Valerian (*Valeriana* spp.) has tranquilizing and sedative properties due to its influences on neuromediators such as γ -aminobutyric acid (GABA; Peeters et al., 2004). There is strong scientific evidence that it decreases CNS activity in mice equal to that of phenobarbital (Hendriks et al., 1985). Valerian is also effective in treating insomnia and other sleep disorders in humans. The mechanism of action starts with valerianic acid inhibiting the enzyme system that causes the breakdown of GABA in the brain. This respective increase of GABA is associated with sedation and a decrease in CNS activity (Riedel et al., 1982; Houghton, 1999).

The components of valerian include valerianic acids, such as monoterpenes and sesquiterpenes, and iridoid glycosides that give the root a sedative and anti-spasmodic activity. In the volatile oil component of valerian, sesquiterpene are responsible for its biological effect (Houghton, 1999). *Valeriana fauriei*, *Valeriana officinalis*, *Valeriana edulis*, and *Valeriana wallichii* are more commonly studied species of valerian. The amount of active ingredient in each depends on the form and preparation of the product (e.g. capsule, tincture, tea, etc.). It has been determined that the highest concentration of valerianic acids were recovered in powder capsules, whereas the lowest amount was found in tinctures and teas (Lefebvre et al., 2004).

No known studies have been done in horses to date, but many ‘calming aids’ or ‘stress relief’ supplements include valerian as one of the major active ingredients (Anon, 2003). With the strong evidence of the sedative effects vale-

rian causes in other species it creates an assumption that it will produce the same effects in horses. Caution needs to be taken when supplementing with valerian however, as certain regulatory organizations, such as the International Equestrian Federation (FEI), and the United States Equestrian Federation (USEF, 2006) ban this product from use during competition.

One study evaluated the effectiveness of a commercial herb product containing *Valeriana officinalis* L. and *Passiflora incarnate* L., in reducing the physiological response to stress in pigs undergoing transportation simulation (Peeters et al., 2004). Data showed that the rise in stress variables (i.e. cardiac response variables including heart rate, ventricular ectopic beats, and sinus tachycardia elevation) during this transportation were significantly reduced. Additionally, the supplement did not affect intermediate metabolites (glucose, lactate, creatine kinase, and nonesterified fatty acids). Therefore, it was suggested that the supplement was effective as a mild sedative with anti-anxiety properties (Peeters et al., 2004). Another study found a mild tranquilizing effect of a 31.6 mg/kg dose of valeranone in rats subjected to an electric shock avoidance test (Rucker et al., 1978).

Yucca

Yucca (*Yucca schidigera*) contains steroid-like saponins, which produce an anti-inflammatory, antioxidant, and anti-spasmodic effects to reduce pain associated with arthritis (Cheeke et al., 2006). The saponins are natural detergents that form stable foams, which contain both fat- and water-soluble components. As much as 10% of the yucca stem contains saponins making it one of the richest sources (Cheeke et al., 2006). Yucca also contains other active components including polyphenols like resveratrol and yuccaols A–E (Oleszek et al., 2001; Piacente et al., 2004). These phenols are exclusively found in the bark and are not present in the mechanical extraction of the yucca extract (Oleszek et al., 2001).

As of the late twentieth century, the only studies performed on the anti-arthritic effects of yucca were in the 1970s by Bringham et al. (1975) who reported that pain and swelling of human arthritic patients were relieved by yucca supplementation. The theory behind this efficacy was due to the activity of the saponins. More recently the potent antioxidant activity of the polyphenols is also thought to give yucca its anti-arthritic properties (Oleszek et al., 2001; Piacente et al., 2004). It has been proven that yuccaols inhibit iNOS, an inflammatory agent that increases during inflammatory responses (Marzocco et al., 2004). Resveratrol along with the yucca phenols was also found to inhibit NF κ B, a transcription factor that controls the expression of iNOS (Tsai et al., 1999).

Yucca has also been proven to have various anti-platelet effects. One study found resveratrol and other yucca phenolics to reduce the level of ROS in blood platelets, along with changes in the production of superoxide radicals,

inhibition of free radicals activated by thrombin, and decreased lipid peroxidation (Olas et al., 2003).

Many equine joint supplements on the market today contain yucca among other anti-inflammatory agents. Many company testimonials and advertisements have theorized yucca to decrease respiratory problems, such as COPD in horses, however no scientific studies have been performed in horses. Studies in other livestock species have looked at ruminal fermentation and metabolism of yucca in sheep (Eryavuz and Dehority, 2004; Santoso et al., 2006) and cattle (Hristov et al., 2003). For a review on research in other animals (chickens, mice, pigs, sheep, cattle, rabbits and quail) and the biochemistry of yucca see Piacente et al. (2005), and for its uses in animal nutrition see Chee and Otero (2005).

Other herbs and functional foods

Black tea, orange peel, and cranberry extracts have been studied in intensely exercising horses (Liburt, 2005; Streltsova et al., 2006). Black tea (*Camilla sinensis*) contains aflavin, a polyphenol, which is a strong inhibitor of the gene expression for IL-8. Black tea extract administered prior to nine horses exercising until exhaustion on a treadmill, decreased mRNA expression of TNF- α and IFN- γ , but produced higher lactate levels throughout exercise compared to the same horses exercised without the supplement (Streltsova et al., 2006). Orange peel extract contains citrus-derived polymethoxylated flavones that have an inhibitory effect on TNF- α expression. The same study in horses found that orange peel extract decreased IFN- γ expression at fatigue, and appeared to decrease recovery time of cardiovascular parameters compared to controls.

Cranberry (*Vaccinium macrocarpon*) polyphenols have been shown to protect endothelial cells against stress-induced up-regulation of oxidative and inflammatory mediators (Youdim et al., 2002). Phenolics in cranberries, like quercetin and cyanidin, have highly effective radical scavenging structures (Zheng and Wang, 2003). Cranberry appeared to attenuate the TNF- α response in nine horses undergoing intense exercise, but not the appearance of IFN- γ (Liburt, 2005). This may prove useful in lessening delayed onset of muscle soreness (DOMS) following strenuous activity.

Herb–drug interactions

Many people believe that because herbs are ‘natural’ products that it also qualifies them as ‘safe’, however evidence of various herb toxicities and negative side effects has shown this to be a dangerous misnomer. Herbs can have a drug-like action that can interact with other components in the horse’s diet. Some herbs contain prohibited substances like salicylates, for example meadowsweet (*Filipendula ulmaria*), poplar (*Populus tremuloides*), willow (*Salix alba*), and wintergreen (*Gaultheria procumbens*), heroin (e.g. poppy, *Papaver somniferum* L.), caffeine (e.g.

cocoa, *Theobroma cacao*), coffee (*Coffea arabica*), Guarana (*Paullinia cupana*), tea (black, green, oolong; *C. sinensis*) and steroids (e.g. ginseng, licorice (*Glycyrrhiza glabra*), hops (*Humulus lupulus*), sage (*Salvia officinalis*)). Drug–herb interactions can create various side effects ranging from mild to severe; thus caution needs to be taken when determining which ‘natural product’ to use.

A general review of various species and drug–herb interactions can be found in Miller (1998) and Izzo et al. (2005). Harman (2002) and Poppenga (2001) have written extensive reviews on the toxicology of herbs in equine medicine. Below is a list of a few known interactions or negative effects, which are also summarized in Table 1.

Valerian components have been found to prolong the action of barbiturates (Dunayev et al., 1987) and can interact with alcohol (Miller, 1998). It has also been shown to inhibit cytochrome P450, the body’s major detoxification enzyme, which can lead to multiple drug interactions if not used with caution (Lefebvre et al., 2004). Echinacea has shown that persistent use is related to hepatotoxic effects and should not be taken with other hepatotoxic drugs like steroids (Miller, 1998; Barrett, 2003). Garlic, along with the potential to cause Heinz Body Anemia in horses when fed in excessive amounts as an extract >0.4 g/kg BW as detailed above (Pearson et al., 2005), was found to create gastrointestinal upset, allergic reactions and dermatitis in humans (Bleumink et al., 1972; Kleijnen et al., 1989). Garlic also decreased systolic and diastolic blood pressure; however, there was insufficient evidence to recommend its use in clinical hypertension (Silagy and Neil, 1994). Ginger has proven to inhibit thromboxane synthetase and increase bleeding time, which could be detrimental if used with anti-clotting drugs like warfarin (Backon, 1986). Some of ginseng’s adverse effects include hypertension, insomnia, vomiting, headache, nervousness, sleeplessness, and epistaxis in humans (Block and Mead, 2003). It is also recommended when utilizing ginseng to discontinue use of corticosteroids, warfarin, heparin, aspirin, and other NSAIDs (Miller, 1998; Poppenga, 2001).

Conclusions

Various herbs are being used in the equine industry, including bee pollen, devil’s claw, Echinacea, flaxseed, garlic, ginger, ginseng, valerian and yucca. Despite many anecdotal reports of efficacy, most of the herbal supplements have never been proven effective in horses; therefore careful consideration must be made when selecting a supplement both for financial and safety reasons. Factors such as the horse’s purpose, breed, age, sex, general health, reproductive status, and current diet including medications, must be taken into account before supplementation. Many herbs have drug-like action and can potentially interact with other medications or dietary component(s). Therefore, if a horse is at risk of developing a potential toxicity or drug

interaction, an equine veterinarian or nutritionist should be consulted.

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