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Use of the Herb Gynostemma Pentaphyllum and the Blue-green Algae Spirulina Platensis in Horses [PDF]

Eleanor M. Kellon, V.M.D.
Equine Nutritional Solutions
58 Maple Farm Road
Ephrata, Pennsylvania, 17522 USA
e-mail drkellon@aol.com

Introduction

While the use of botanicals/herbs and other naturally occurring substances is considered by many to be little more than folklore, there is growing interest in subjecting these remedies to the hard hard light of modern science in an effort to validity of therapeutic claims and define their chemical composition. Some fail the test, others emerge confirmed as not only useful but sometimes in ways in that have no counterpart in available pharmaceutics. I would like to describe two such "natural" therapies and my experience with them in horses.

Gynostemma pentaphyllum – Description and Effects

Gynostemma pentaphyllum (Jiaogulan, Jiao Gu Lan Chinese name, aka Amachazuru), is a vine indigenous to mountainous areas of Southern China and other parts of Asia. Although descriptions of it as a medicinal herb date back to the Ming Dynasty (1368-1644 A.D.), it was not widely known or used, even in China, because of the remote locations where it grew. Locals used the vine as a vegetable or tea.

The list of traditional medical uses for the vine is extensive. Thanks to growing interest in China in documenting therapeutic claims for herbs by scientific investigation to determine clinical effects and identify active principles, several studies have now been completed. The active components are flavones and gypenosides. The gypenosides are dammarane type saponins, which have a structure similar to mammalian corticosterone and sex hormones. Table I is a list of Gynostemma effects of most interest to the equine.

Table 1. Effects of G. pentaphyllum of potential use in equines

? Antioxidant protection
? Nitric oxide modulation
? Bronchodilation
? Adaptogen/performance

Anti-inflammatory/Antioxidant: Gypenosides have been found to protect white cells in vitro from elevations in superoxide anions and hydrogen peroxide caused by exposure to zymosan, and to protect liver microsomes and vascular endothelial cells from lipid oxidation triggered by iron and other oxidizing agents (Li 1993). One murine (Cheng 1998) and 2 human (Lu 1998, Liu 1994) in vivo studies have documented the ability of Gynostemma to increase endogenous production of superoxide dismutase and decrease levels of malonaldehyde, a marker of lipid peroxidation, both in toxicity states (fluorosis) and as a consequence of aging.

Nitric oxide modulation: Since the discovery in 1977 that the simple gas nitric oxide (NO) functions as a signaling molecule in the body, thousands of studies have been performed to elucidate its actions both in health and disease. Several different NO generating enzyme systems have been identified, 2 of the most important being: the physiologically active eNOS, endothelial nitric oxide synthetase in the cells lining blood vessels, critical to maintaining vasodilation; and the iNOS system, inducible nitric oxide synthetase, located in the tissues and immune system cells and responsible for the release of large amounts of NO in inflammatory conditions. Gynostemma has been found to be a potent inducer of the eNOS enzyme (Tanner 1999). It also has the ability to suppress the inflammatory iNOS enzyme. (Aktan 2003).

Bronchodilation: One of the oldest recorded medical uses of Gynostemma is the treatment of coughs, respiratory infections and chronic bronchitis. The recent discovery (Circosta 2005) that it decreases bronchial resistance at baseline, inhibits bronchoconstriction in response to histamine by 68%, and inhibits bronchoconstriction in response to antigen in sensitized guinea pigs by 80% provides some insight into beneficial pulmonary effects.

Adaptogen/Performance: Adaptogens are herbs that have the potential to modulate the response to stressors such as disease, infection or exercise. The mechanism of action is not entirely clear, but may be related to the ability of the dammarane type saponins to bind to hormone receptors. For example, some dammarane saponins from ginseng will result in mildly elevated cortisol levels when given to normal mice, but can also protect from high cortisol release associated with severe stress such as immobilization (Kim et al 2003). It is believed this is the result of ginsenoside binding to ACTH receptors on the adrenal gland, causing mild cortisol release under conditions of low ACTH, but dampening the response to high ACTH levels. Gynostemma is not as well studied in this regard as other well recognized adaptogens, but one in vivo Chinese study involving 300 atheletes who were given Gynostemma 30 minutes prior to competition reported subjective improvements in mood, energy level and feelings of fatigue, with decreased anxiety. This requires further investigation.

Toxicity

Gynostemma has been used as both a beverage and a vegetable in indigenous areas for centuries with no recognized ill effects. Formal toxicity testing in rats (Attawish 2004), given dosages as high as six times the equivalent high dosage range used for humans for six months (equivalent to at least 10 years of human use) found no evidence of toxicity. Formal toxicity testing has not been performed in horses. I personally have used dosages as high as 5000 mg/day of whole herb for 2 years with no clinical or biochemical evidence of toxicity. Because of the vasodilatory potential of this herb, use of drugs with a vasodilatory and/or hypotensive action (e.g. Acepromazine) should be done with caution. Because of the potential for antiplatelet effects, use of drugs or other herbs with anticoagulant effect should be done with caution.

Gynostemma pentaphyllum for Laminitis

The anti-inflammatory/antioxidant and oxygen free radical scavenging properties of this herb make it appealing as a laminitis therapy, but more directly pertinent is the potential to modulate nitric oxide production, decreasing iNOS activity while enhancing eNOS. While researchers have yet to unravel all details of the pathophysiology, in acute laminitis a considerable body of evidence points to increased vascular resistance causing shunting of blood away from capillary beds, resulting in tissue hypoxia and subsequent reperfusion injury to the laminae. An imbalance between the vasodilating effects of NO and the potent vasoconstricting actions of endothelin-1 (ET-1) has been proposed as a key factor in the vascular events. Under experimental conditions, infusions of ET-1 cause marked digital vasoconstriction and hoof pain, while use of ET-1 antagonists prevents or reverses this (Katwa et al 1999, Eades et al 2002, Stokes 2003). Concentrations of ET-1 in the laminar tissues of horses with chronic laminitis have been found to be 7 times higher than that of control horses (Katwa et al 1999), indicating an ongoing excessive production of ET-1 in horses with chronic laminitic hoof pain. Induction of iNOS has also been suggested to play a role (Bailey 1999).

Increasing intravascular nitric oxide has received some attention as a therapy for acute lamintis. Huff et al 1990 acclimated horses to a hot environment then followed hoof wall surface temperatures after exposing them to cold with and without the application of topical glyceryl trinitrate and found no effect, and in experimental black walnut induced laminitis (Adair et al 2000) it was ineffective in restoring blood flow to the hoof when treatment was delayed until after the onset of lameness. However, earlier studies (Hinkley et al, 1996) using quantitative near infrared spectroscopy did find increased digital perfusion in both normal and laminitic animals using either topical glyceryl trinitrate or intravenous L-arginine, the precursor amino acid for nitric oxide production. Conflicting results in acute laminitis may be due to a variety of factors, including the model used, the sensitivity of detection methods for laminar blood flow, and the stage of laminitis, where the therapy may contribute to what is already an overabundance of nitric oxide from iNOS induction by tissue damage and inflammation (Hunter RP 2002).

My experience with Gynostemma focuses on chronic laminitis in horses known to be hyperinsuilnemic and presumably insulin resistant. The mechanisms underlying increased laminitis risk in IR horses have yet to be elucidated, but have been proposed to be similar to those which cause vascular disease and hypercoagulability in human IR.(Johnson 2002). In the human condition, markers of chronic inflammation including overproduction of reactive oxygen species (Busija et al 2005), while overexpression of iNOS (Barbata et al 2005) and ET-1 (Lteif 2004) have been identified as pathophysiological factors. The ability of Gynostemma to suppress iNOS activity while enhancing eNOS demonstrated in vitro made it appealing as a potential chronic laminitis therapy.

To date, 176 horses have been followed for a period of from 3 months to 2.5 years after starting Gynostemma. As mentioned, these horses were confirmed to be hyperinsulinemic with normal blood sugars. Study inclusion criteria were strict, and designed to guarantee that all possible measures had already been taken to control the hyperinsulinemia and properly care for the feet. These are detailed in table 3.

Table 2. Recommended pre-requisites for use of Gynostemma in chronic laminitis

? Use of pergolide if the animal was also positive for pars pituitary intermedia dysfunction ? Use of an appropriate, low NSC, mineral balanced diet (Johnson et al 2004) ? Regular and appropriate hoof care ? History of ongoing lameness for a minimum of 6 weeks following an acute laminitis episode, despite the measures above ? Use of phenylbutazone, other NSAIDs or potentially vasoactive drugs to be discontinued

Study animals were horses and ponies of various breeds, mares and geldings, with a slight preponderance of mares (57%), ranging in age from 3.5 years to 29 years. 132 (75%) of the study horses had been judged to require ongoing NSAID therapy for pain control prior to the start of the study. Dosages ranged from 1000 to 2000 mg of Gynostemma powder/227 kg (500 lbs) of bodyweight, twice a day. Observed effects included more mental alertness and increased spontaneous movement. A pinker color to oral mucus membranes and tongue was consistently observed, presumed to be a reflection of increased vasodilation. These responses were used to determine when a therapeutic dose had been reached. 109 (61.9%) returned to pasture soundness at a walk with 2 days to 2 weeks of starting the Gynostemma. Surfacing of abscess collections is very common during the initial 2 to 3 weeks of treatment. 20 (11.4%) were nonresponders. No response was associated with poor control of the underlying medical problems or severe demineralization of the coffin bone. The remaining 47 animals (26.7%) showed improvement of 1 to 2 lameness grades. Amount of rotation of the coffin bone and degree of lameness at the start were not predictive of response. No side effects were observed.

Gynostemma and Spirulina for horses

Inflammatory airway disease is a common problem in high performance horses, resulting in bronchoconstriction with the potential to negatively impact performance, even when subclinical (Pirrone 2005). While there are many effective medications, they are prohibited in performance horses. The bronchodilator effect in other species makes Gynostemma a potential therapy. In 2 cases, it was combined with Spirulina platensis, 20 grams twice a day, the equine dose equivalent to achieve antihistaminic effects in humans. Spirulina is a blue green algae with documented (in vitro and in vivo in laboratory animals) potent antihistaminic (Chen et al 2005, Remirez et al 2002) and immunomodulating capacity (Hyashi et al 1998, Nemoto-Kawamura et al 2004) but with a high safety profile, being used as a dietary staple in some areas of the world, and by the World Health Organization as a protein supplement for malnourished children in underdeveloped nations. The immunomodulating effect involves a shift in antibody class toward IgG and IgA, and away from IgE.

Case studies:

Case 1. 8 YO mare, Warmblood event horse, with chronic cough during exercise, and poor respiratory recovery rates after even moderate exercise. Bronchoalveolar lavage (BAL) showed high numbers of mast cells. She was poorly responsive to clenbuterol or corticosteroids. Dietary and bedding changes had not resolved the problem. She was started on 2000 mg of Gynostemma and 20 grams of Spirulina, twice daily. Within 48 hours, her respiratory recovery rates had normalized. Coughing stopped within a week. At 6 month follow up, she continued to be symptom free.

Case 2: 2 YO Standardbred filly, with clear to slightly frothy nasal discharge, worse after work, poor respiratory recovery rates at all levels of work, difficulty finishing the last quarter of training miles, unable to train down below 2:27. BAL consistent with inflammatory airway disease. She was started on

2000 mg Gynostemma 30 minutes to 1.5 hours before exercise. Recovery rates normalized after the first dose. Two days after starting the herbs, she trained in 2:25, then 5 days later in 2:21 with ease and rapid respiratory recovery post training.

Case 3. 4 YO Standardbred gelding with weak finishes racing, seasonal headshaking accompanied by snorting and sneezing beginning early April. Occasional cough. Endoscopy revealed patchy mucus with normal appearing respiratory mucosa. BAL consistent with inflammatory airway disease. History of multiple courses of various antibiotics with no improvement. Improved respiratory recovery rates with clenbuterol but illegal for racing. Started on 10 grams Spirulina with 1000 mg Gynostemma twice a day with partial response, increased to 20 grams Spirulina and 2000 mg Gynostemma twice a day with complete cessation of headshaking and sneezing, normalization of respiratory recovery rates, stronger last quarters and a win with a new lifetime mark, improved by 1 second.

The same changes in level of alertness, energy level and pink color of the gums and tongue, as seen in the horses on Gynostemma in the laminitis trial, was observed. The higher energy level manifested as enthusiasm for work, not nervousness or jumpiness.

Determining dosage

Regardless of how promising an herbal may look based on research, there is always difficulty with transposing the data to horses when no information exists on how this species may respond. While many aspects of physiology are preserved across mammalian lines, species differences certainly exist and effects are not necessarily predictable. Another problem is that studies may use intravenous or intraperitoneal routes of injection, or purified and standardized concentrations of one or more active chemical constituent.

On a metabolic bodyweight basis, human oral doses can be transformed to adult equine equivalents by multiplying by a factor of 4 to 6. Commonly used human dosages of actual gypenosides are 20 to 60 mg, usually 3 times daily. Ground whole herb is generally the most economical form to use in the horse. The gypenoside content of Gynostemma pentaphyllum ranges from as high as 15 to 20% for the wild type (rarely available outside China) to 5% for cultivated herb, which is the type most often available commercially. Therefore, at the lower end of gypenoside content the amount of whole herb required for a dose of 100 mg of gypenosides, 5 times the human low end dosage, would be 2000 mg. When using an herb for the first time in a horse, I generally will start with half that dose, as was done in the laminitis study below. Many of the insulin resistant horses proved to be quite sensitive to the effects and responded well at this low dosage, while the racehorses required higher dosages.

A final problem with dosing of whole herbs is that you need to identify a supplier who provides consistent quality shipment to shipment. Bulk suppliers generally deal with a limited number of steady sources, eliminating wide variations in chemical composition of the herb that may be related to different geographical areas. Some natural variation is still to be expected depending on weather conditions but in the 3 years I have been ordering Gynostemma pentaphyllum from the same bulk herb supplier it has produced consistent and reliable results with no need for dosage adjustments. An alternative to whole herb is using a human product with a standardized gypenoside content, in which case dosage may be adjusted depending on the known concentration.

Table 3. Dosage determination steps

I. Low end human dose = 20 mg of actual gypenosides. To convert to equine (500 to 550 kg) on a metabolic bodyweight basis, multiply x 5 = 100 mg of actual gypenosides
II. For whole herb, assume lower end gypenoside concentration for untested herb = 5% gypenosides. For target dose of 100 mg, divide by 0.05 = 2000 mg
III. When using a standardized human product, whole herb or extract, use the known concentration to determine dose; e.g. For a human product containing 20 mg total gypenosides per tablet or capsule, 100 mg divided by 20 mg./capsule = 5 capsules
IV. When using an herb for the first time in a horse, it is generally advisable to start with lower then predicted doses and increase gradually to determine response.

I have also used Spirulina alone for control of allergic respiratory symptoms in horses that are not in hard work, and for skin hypersensitivity reactions such as Culicoides reactions, “sweet itch”.

A similar wide dosage range has been suggested for Spirulina platensis in human allergic conditions. Again, the lowest recommended human therapeutic dose, 3 grams, was increased by a factor of 5 to 15 grams. 10 grams twice daily was tried first, then 15, with failure to obtain optimal relief of symptoms. 20 grams gives consistent symptomatic relief in horses from 950 to 1200 lbs. Dosage may be adjusted up or down for smaller and larger horses, respectively.

Summary

As interest continues to grow in investigating natural remedies by scientific methods to determine their effects and the pharmacology behind them, we can finally move from the realm of anecdotal evidence or unfamiliar systems of medicine into an arena where the choice of an herbal remedy becomes in essence the same as a choice of drugs. This opens a wide vista of potential therapeutic tools, often with unique properties to offer, such as Gynostemma's simultaneous suppression of iNOS while supporting eNOS activity, and the potential for Spirulina platensis to simultaneously exert an antihistamine effect by stabilizing mast cells and a shift in immunoglobulin production away from IgE. There are many possible pitfalls, including difficulty in extrapolating data across species and determining equine appropriate dosages, and we are a long way from establishing an equine specific herbal database, but the incorporation of plant based therapies into the equine treatment arsenal holds great promise.

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