A Study of Equine Ulcers and Dietary Supplements

Ulcers in horses are ubiquitous, but a unique formulation of natural ingredients can reduce their size and number.

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Introduction

Franklin L. Pellegrini, DVM, and Scott C. Anderson

Studies over the past decade have documented an unsettling fact: over 90% of racehorses and 60% of show horses have gastric ulcers (McClure et al., 1999). Worse yet, the number one killer of horses is colic (Traub-Dargatz et al., 2001), which is an expensive and unnecessary tragedy.

This unfortunate state of affairs, known as equine gastric ulcer syndrome (EGUS), is due to the heavy training and unnatural feeding regimens employed to maximize performance. Horses in the wild graze in herds all day and only sporadically exert themselves, but stabled race and show horses are kept in confinement and fed high-carbohydrate feed two or three times a day in order to increase their performance. Carbohydrate loads in excess of what the small intestine can absorb continue to the hindgut, where a portion of them are fermented by bacteria into lactic acid, which can lead to hindgut acidosis (Richards et al., 2006).

Unlike humans who secrete digestive juices on demand, horses secrete stomach acids on a fairly continuous basis. As they eat, they swallow bicarbonate-containing saliva at the rate of five gallons a day, helping to neutralize these stomach acids. When they eat only two or three times a day, there is far less saliva to buffer the gastric juices, which include hydrochloric acid, bile, and pepsin, and can reach a highly acidic pH of 1.5. Research done at the University of Florida has shown that heavy training may then move these acids around to less protected parts of the stomach (Lorenzo-Figueras and Merritt, 2002).

This establishes an unnatural stomach environment that may ultimately lead to ulceration. Horse ulcers are most prevalent in the upper, squamous area of the stomach and the margo plicatus, but they are often found in the glandular lower section as well (Mair et al., 2008). These ulcers in turn lead to loss of blood, irritability, and poor absorption of nutrients. Paradoxically, this may negatively impact the performance of exactly those horses which are expected to work at peak efficiency. Ulcers may be responsible for much of the subclinical anemia, listlessness, weight loss, and general poor health noted by many performance horse veterinarians for years. In fact, the number one complaint about horses with ulcers is that their performance is declining (Mitchell, 2001). With these animals, environment has a much larger impact on their ability than genetic factors (Kronfeld, 2003).

Gastric ulcers in horses can be inspected by endoscopy, but colonic ulcers are much harder to observe. Colonoscopies are impractical due to the difficulty of evacuating the equine colon without endangering the health of the horse. Lacking evidence to the contrary, it has generally been felt that equine colonic ulcers are rare.

This paper reports on two recent studies that cast a worrying light on equine ulcers, demonstrating that in addition to gastric ulcers, horses are also plagued by colonic ulcers, afflicting over 60% of performance horses.

Additionally, one of these studies indicates that the most commonly prescribed drugs for treating gastric ulcers has little or no effect on colonic ulcers. Finally, this paper discusses a novel feed supplement that has been shown to reduce both gastric and colonic ulcers in performance horses.

Functional Feeding and Equine GI Health

By Peter M. Bedding, PhD, and Scott C. Anderson

Feeds are not medicines, but good feed management is probably the best long-term solution to many digestive problems, including ulcers. Ironically, feed is also the main culprit in many of these disorders. This is because trainers often put their horses on hard feed in order to guarantee high energy concentrations for maximum performance. But in addition to giving them extra energy, hard feeds also allow large quantities of sugars to be released in the mouth.

Horses have evolved to eat large quantities of grass, and in the process they produce gallons of saliva daily. But when it is allowed to chew only small amounts of hard feed, a performance horse doesn't generate enough saliva to buffer the high levels of sugars and acids that are produced.

As well as decaying their teeth, the hard feed adds to the acidity of the stomach, which in due course challenges the stomach wall. Together with stress and exercise, this can lead to stomach ulcers.

A natural diet supplies substances that support the integrity of the GI tract. However, in emphasizing performance, many manufactured feedstuffs end up being deficient in naturally occurring nutricines that are needed to maintain the health of a horse.

Vitamins and minerals are typically added in an attempt to correct these shortcomings. When various nutricines are compounded to address a specific function—such as immune response or tendon healing—it is called functional feeding, and the formulation is called a nutraceutical. But before any functional feeds can have an effect, the gut itself must be in good shape. Therefore, a nutraceutical that addresses the proper functioning of the gut provides a necessary foundation for all other functional feeds.

Such a gut-oriented functional feed would include specific prebiotics, amino acids, nucleotides, polar lipids, and antioxidants. With a nutraceutical like this, the health of the GI tract can be actively managed, protecting the gut wall from attack by acids, pathogens, and toxins and promoting the regeneration of intestinal tissue cells.

Pasturing a horse is a sure-fire way to improve its digestion, but it doesn't provide the energy density needed for a performance horse. In the absence of the ideal natural feeding environment, a functional feed is essential.

In today's high-performance horse world, ulcers are ubiquitous and colic is the number one killer. But with the proper functional feeding program, the equine GI tract can quickly recover from insults even during strenuous training, allowing the horse to operate at the absolute peak of its abilities.

A Large-Scale Necroscopic Study

Franklin L. Pellegrini, DVM, and Scott C. Anderson

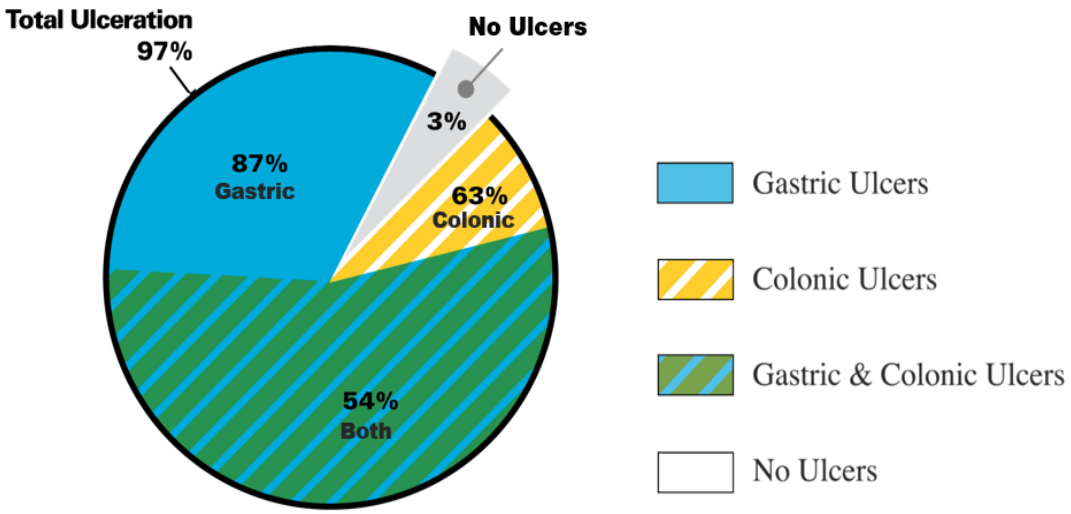
In 2003, one of the authors (Pellegrini) conducted a large-scale necropsy on 180 performance horses in a Texas abattoir. It was found that 87% of these horses had gastric ulcers and 63% had colonic ulcers, resulting in an overall ulceration rate of 97% (Pellegrini, 2005). These results were then correlated to a guaiac-based Fecal Occult Blood Test (gFOBT).

After being euthanized, necropsies were performed on the horses. Gastric ulcers were observed and graded on a standard scale of 0–4, as described below:

- **Grade 0:** Normal, unulcerated tissue. The epithelium is intact and there is no thickening or abnormal coloring.
- **Grade 1:** The mucus lining is intact, but there are areas of thickened, discolored tissue.
- **Grade 2:** Small, single, or multiple ulcers present.
- **Grade 3:** Large, single, or multiple ulcers.
- **Grade 4:** Extensive, deep ulcers.

Colonic ulcers were also observed and—lacking an accepted standard of measurement—were marked as either extant or not.

The results may be summarized by the following graph:



Incidence of gastric and colonic ulcers. Note the large overlap representing horses with both gastric and colonic ulcers. Only 3% of horses have no ulcers.

Prior to the dissection of the horse, a fecal sample was collected. This manure was tested with guaiac and correlated to the gross examination of intestinal tissue.

Overall, the guaiac test proved to be highly specific and significant (100% for both, with P=0) for the existence of an ulcer, due to the unexpected lack of false positives in this group. The existence of false negatives, however, lowered the overall accuracy of the test to 65%, roughly comparable to human outcomes with such a test.

Guaiac works by binding hemoglobin and turning blue in the presence of hydrogen peroxide. The false negatives are likely due to the fact that the guaiac reaction is not very sensitive, requiring 10mg of hemoglobin per gram of stool to produce a positive result. Since many ulcers bleed only lightly or sporadically, these may be missed by the gFOBT.

Importantly, this study demonstrated that when there is a positive gFOBT in the absence of gastric ulcers, then colonic ulcers are always present. Thus, endoscopy in combination with a gFOBT can provide a significant test for colonic ulcers.

A Comparative Study

By Franklin L. Pellegrini, DVM, and Scott C. Anderson

In order to evaluate the effectiveness of a novel feed supplement containing oat- and yeast-based nutraceuticals, an 80-horse study was conducted at an Ohio Standardbred racehorse stable. For the test, 20 horses were assigned randomly to each of four groups, including a control, a group using proton pump inhibitors, and two groups that were administered different dosages of the feed supplement.

Proton Pump Inhibitors

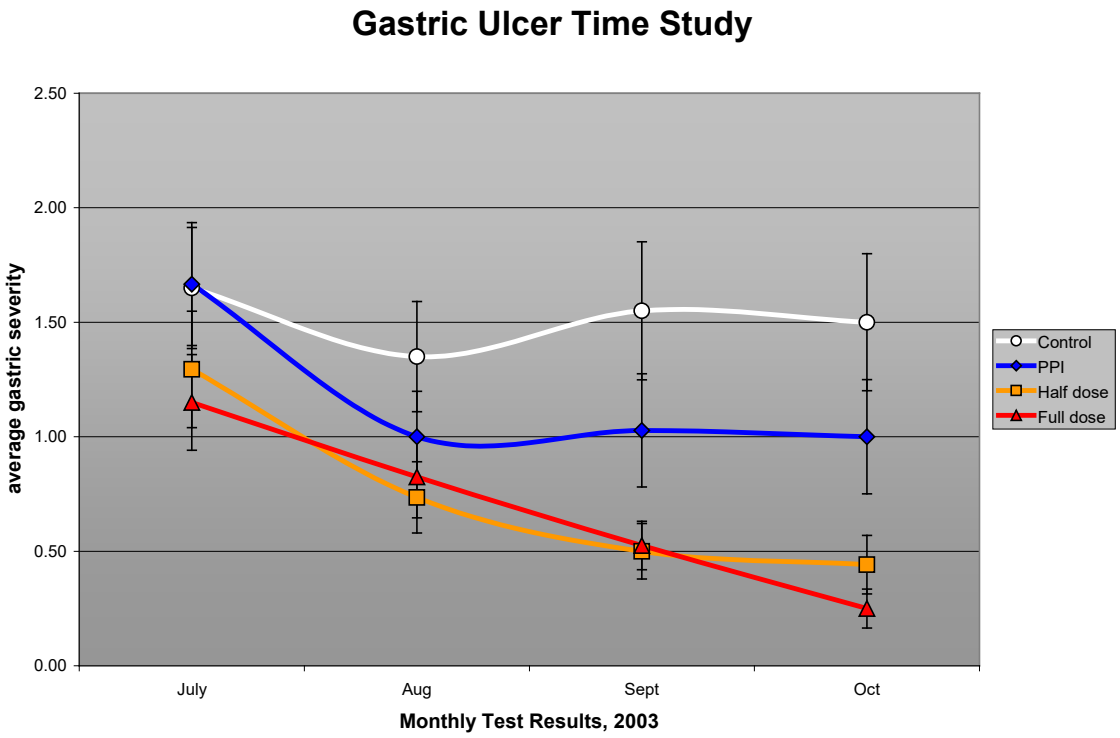
Proton pump inhibitors (PPIs) are a class of drugs that block the production of stomach acid. These are typically prescribed for horses that are known by endoscopy to have ulcers, but are also prescribed for non-specific ailments on the theory that if improvement is noted, then an ulcer was likely to blame.

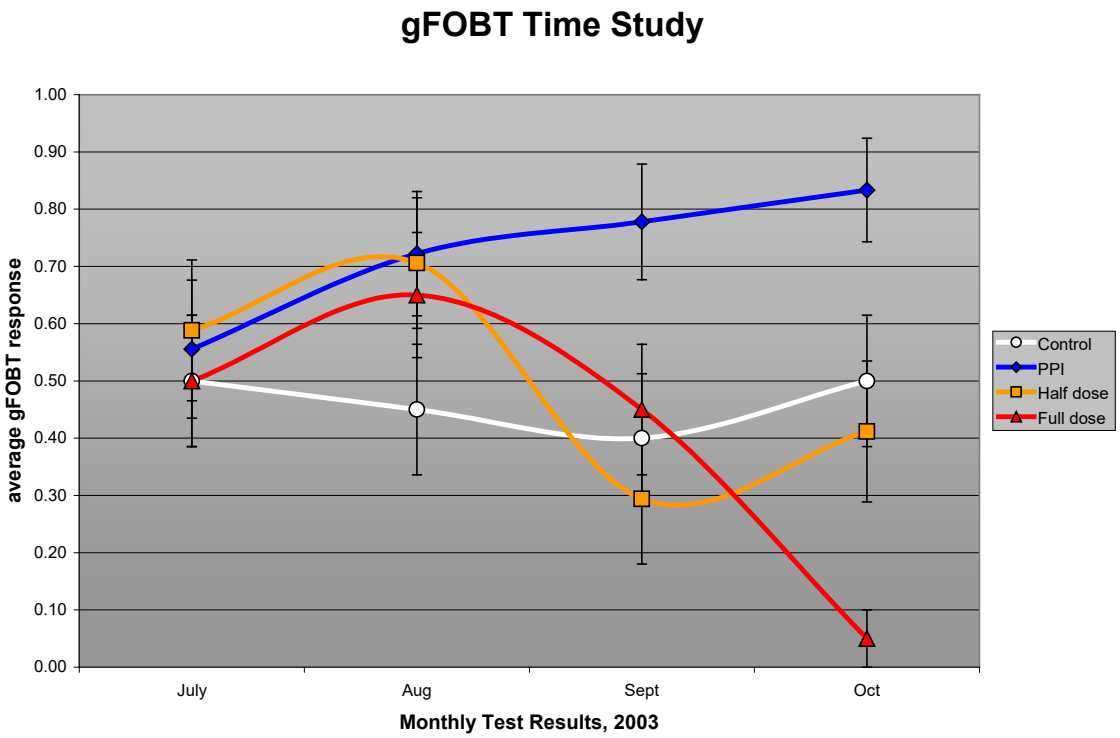
In a blind test of 20 Standardbred horses on a proton pump inhibitor vs. 20 controls, it was found that acid inhibition was effective at reducing gastric ulcer severity (graded on a scale from 0–4) in the first month of treatment as determined by endoscopy.

This comparative study also looked at the effects of two different dosages of an oat- and yeast-based nutritional supplement (SUCCEED DCP) on the rate of ulceration. Using two other groups of 20 horses each, DCP showed a dosage-dependent improvement in gastric ulcers, reducing the average severity to less than 0.5 by the end of the study (error bars show standard error, adjusted for population size).

During the period of this study, a guaiac-based fecal blood test (gFOBT) of the manure was also conducted. The guaiac test can produce false positives when exposed to blood from eating red meat; fortunately, this is not a problem for herbivores. Nevertheless, it has been suggested that the guaiac test might be skewed toward false positives in horses as well, perhaps due to chlorophyll or other peroxidase-mimicking molecules in their feed. However, in an independent (unpublished) Texas study we found both gastric and colonic ulceration correlated with a high significance and specificity to a positive guaiac stain.

Interpreted in this light, the gFOBT data can serve as a proxy for colonic and other non-gastric ulcers. The study demonstrated an overall dosage-dependent reduction in these non-gastric ulcers for horses using the nutritional supplement. Proton pump inhibitors, which are specifically designed for gastric ulceration, did not show a decrease over this time period.


Gastric Ulcer Time Study
average gastric severity
2.50
2.00
1.50
1.00
0.50
0.00
July
Aug
Sept
Oct
Monthly Test Results, 2003
Control
PPI
Half dose
Full dose


gFOBT Time Study
average gFOBT response
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
July
Aug
Sept
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Monthly Test Results, 2003
Control
PPI
Half dose
Full dose

These dosage-dependent results are a strong indicator of the efficacy of DCP for reducing fecal blood, a proxy for colonic ulcers in performance and racehorses.

Further studies are planned, using a more sensitive ELISA (enzyme-linked immunosorbent assay) test, to better analyze the presence and extent of colonic ulcers.

Conclusions

This paper has several findings:

- Not only do horses have gastric ulcers, they also have a high incidence of colonic ulcers.
- Proton pump inhibitors are useful to quell gastric ulcers, but they have little effect on colonic ulcers.
- A nutritional feed supplement made with oat oil, oat flour, amino acids, nucleotides, and yeast extracts, including mannan oligosaccharides (SUCCEED DCP), has been shown to deliver a strong dosage-dependent reduction in both gastric and colonic ulcers.

Next Steps

Further research is scheduled to investigate anecdotal reports of improved equine disposition, appearance, performance, and reproductive success. In addition, a more sensitive ELISA test is being developed that will be used in a follow-up necroscopic study of equine ulceration.

A Nutritive Supplement for Horses

Peter M.J. Bedding, PhD, and Scott C. Anderson

In order to treat these gastric and colonic ulcers in horses, one of the authors (Bedding), devised a feed supplement to target each aspect of the problem. The hope was to create a digestive conditioning program that would normalize conditions in the GI tract while still allowing horses to be rigorously trained.

This feed supplement was subsequently tested on 80 horses in Ohio. The key ingredients of this patent-pending formula include:

Polar Lipids

Lipids represent a large class of molecules that include fatty acids, phospholipids (lecithin), galactolipids, and triglycerides. They play a key role in the structure and function of cellular membranes and are found in much of the plant material already in equine diets. As a consequence of their ubiquity, lecithins and lipids are considered to be a GRAS (generally regarded as safe) supplement.

Oat oil is rich in polar lipids, particularly galactolipids. These are rare in animals, but are the most common lipids in plants, as well as the most abundant form of lipids on the planet. Animals generally lack the enzymes needed to synthesize these polyunsaturated polar lipids, and so they must acquire them in the diet. These dietary polar lipids are important in forming the tight junctions between the epithelial cells lining the gut. Cells connected in this fashion present a unified barrier against digestive juices, toxins, and pathogens. When these junctions are disrupted, the defensive wall is breached, and injury in the form of an ulcer may result. Adding polar lipids to the diet has been shown to protect the intestinal mucosa and to strengthen the impermeability of the barrier (Martin et al., 1981; Kiviluoto et al., 1991; McNeil and Ito, 1989).

As well as galactolipids, oat oil is rich in trienols and tocopherols, powerful antioxidants that sweep free radicals out of the system before they can damage the surrounding tissue.

Polar lipids are versatile emulsifiers, stabilizing oil-water mixtures. They provide an ideal nutrient delivery vehicle, capable of ferrying both fat- and water-soluble molecules into the tissues. Fat-soluble nutrients include vitamins A, K, D, and E. Polar lipids, especially galactolipids, have been shown to increase bioavailability of such nutrients by up to 500%.

After transporting their nutritive load, polar lipids are readily absorbed in the gut (after digestion by bile salts), where they supply extra energy to the horse (Kreitler, 2003).

Beta glucan

Beta glucan is a polysaccharide: a chain of glucose molecules that can branch in specific conformations, each one having unique properties. This branching is represented by a beta notation that describes how the chains are linked, such as β(1,3). Different beta glucans can be derived from yeast, barley, and oats, and they can have profound effects on typical animal

systems. They have been known for years to reduce LDL cholesterol levels in the blood (Davidson et al., 1991; Bell et al., 1999).

More significantly, beta glucans moderate the release of sugars from the digestive system, helping to prevent the sugar highs and lows that often afflict animals that are fed only two or three times a day on an energy-rich, high-carbohydrate diet (Braaten et al., 1994). Studies have shown that beta-glucan is effective in reducing post-prandial glycemic peaks by up to 50% (Tappy et al., 1996).

Although more equine studies are needed, research has implicated bacteria in the formation of ulcers in many animals. While it has been difficult to culture bacteria from horse stomachs, colonic bacteria are generally known to include a wide variety of pathogenic species.

Beta glucan is a potent stimulator of the immune system. It arouses macrophages—which have a specific beta glucan receptor—to fight pathogenic microbes, mitigating infection and allowing damaged tissue to heal (Czop, 1986; Estrada et al., 1997; Reid et al., 2004).

Physically, beta glucan creates a gel, slowing the transit of feed through the gut and allowing starches to be digested earlier in the system, thereby reducing the negative effects of starch in the hind gut (Böhm and Kulicke, 1999; Wursch and Pi-Sunyer, 1997).

Freedom Health uses beta glucan derived from oats, β(1,3/1,4), as well as yeast β(1,3). The beta glucan from oats is mainly soluble, while the beta glucan from yeast is mainly insoluble. Beta glucans of the form β(1,3) have the greatest immunomodulatory effect.

Glutamine (outside E.U.)

Glutamine is the most abundant amino acid in humans as well as horses. Glutamine deficits can result in diarrhea, villous atrophy, mucosal ulceration, increased intestinal permeability, and necrosis (Roth et al., 1996).

Glutamine is a muscle fuel and also supplies nitrogen to the immune cells of the intestinal mucosa, which help to prevent pathogenic organisms from entering the circulatory system. Glutamine is considered to be a nonessential amino acid under normal conditions, because the body can create as much as is needed from scratch. But when the digestive system is stressed—for instance by ulcers or malnutrition—large amounts of glutamine are consumed, and supplements may be needed to replenish the supply (Duckworth et al., 1992; Vasquez et al., 1996).

Arginine (E.U. Only)

Arginine is a conditionally essential amino acid, associated with a healthy gut lining and rapid wound healing. Arginine is a precursor to nitric oxide (NO), which dilates blood vessels and improves circulation (Moncada and Higgs, 1993). This improved circulation has been shown to enhance reproductive performance in mares and other animals, shortening the gestation period and increasing uterine arterial blood capacity (Mortensen et al., 2011).

Arginine, along with glutamine, enhances gut function (Stechmiller et al., 1997). Arginine also decreases mucosal injury following pathogenic invasion and shortens recovery time following illness or intestinal wounding (Sukhotnik et al., 2004). It stimulates the production of T cells, enhancing the immune response (Madden et al., 1988; Gianotti et al., 1993).

Importantly from the viewpoint of performance athletes, arginine increases the production of growth hormones and insulin, leading to enhanced strength and stamina (Sureda and Pons, 2012; Schmidt et al., 1992).

Threonine

Threonine is an essential amino acid and an important component of the mucin produced by the goblet cells distributed throughout the intestinal tract. By assisting metabolism and nutrient absorption, threonine contributes to a smoothly functioning GI tract. A deficiency of threonine slows the regeneration of the gut wall and depresses the production of mucus (Bertolo et al., 1998; Ball et al., 1999).

Threonine is especially useful for wound healing and for treating stress, but it is also an essential link in the production of immunoglobulins (Cuaron et al., 1984).

Nucleotides

Although the GI tract is covered in mucus, the acids and enzymes nevertheless take a toll on the enterocytes lining the gut wall. The cells there are constantly dividing, ultimately managing to totally replace the intestinal lining about every three days.

This continuous cell division requires the replication of millions of DNA molecules every second. In turn, each DNA molecule is made up of several billion nucleotides. This represents an impressive amount of energy-intensive chemical synthesis. Clearly, maintaining an adequate level of nucleotides is a major, ongoing problem for the digestive system.

In general, DNA is synthesized through a complicated pathway that creates fresh nucleotides de novo. However, in the presence of pre-made nucleotides, the body can down-regulate this synthesis and instead use an enzyme named HGPRT to scavenge the intact nucleotides, improving the efficiency of cell repair.

In addition to simple maintenance, cell division is also critical for the repair of damaged tissue, including ulcers. DNA synthesis is thus a limiting factor in the healing process as well.

In times of stress, certain cells of the digestive system—including the mucus-producing goblet cells—are incapable of meeting the increased demand for nucleotides. Under these conditions, nucleotide supplements in the diet have been proven to be beneficial. Studies have shown that nucleotide supplements increase mucosal thickness and protein levels and speed up intestinal recovery after chronic diarrhea and intestinal damage (Bueno et al., 1994).

Nucleotide supplements have been shown to increase the maturity and growth of normal enterocytes while reducing their dependence on exogenous glutamine (Uauy et al., 1990). The

mechanism for this is not totally understood, but for intestinal villi to grow, stem cells in the crypts must divide and push their way up the length of the villi (Marshman et al., 2002). Exogenous DNA may enhance this process, perhaps explaining the extra crypt depth and increased surface area noted with nucleotide supplements.

Dietary nucleotides also seem to have an important beneficial effect on the intestinal microflora, stimulating the growth of beneficial bacteria and inhibiting pathogens. This may be due to yet another effect of dietary nucleotides reported in a NASA study and elsewhere: stimulation of the immune system (Hales, 2001; Lin, 1995). In particular, lymphocytes and erythrocytes are not able to synthesize the purine-based nucleotides at all. For these cells, available nucleotides are essential to proper functioning.

Yeast Products

Saccharomyces cerevisiae is a species of yeast with a long history in health and gastronomy. It has several beneficial properties, two of which are incorporated into SUCCEED DCP.

Yeast Beta glucan

As discussed earlier in the section on beta glucan, yeast beta glucans are of the form β(1,3) and are potent immunomodulators. Yeast beta glucan is extracted from the inner cell wall of the yeast cell. It is also an efficient mycotoxin adsorbent, helping to minimize the effect of mycotoxins produced from fungi and molds found in contaminated grain, forage, and feeds.

Mannan Oligosaccharides

Mannan oligosaccharide (MOS) is a polysaccharide composed of chains of the sugar mannose. It is extracted from the outer cell wall of *S. cerevisiae*. It binds to projections called fimbria on bacteria such as *salmonella* and *clostridia* (Ip and Lau, 2004). Thus bound, fimbria can't form connections with enterocytes, preventing infection. The bound bacteria are then flushed from the system (Swanson et al., 2002). The result is a positive modulation of gut microflora and reduced risk of infection.

MOS can be digested by the enzymes of certain beneficial bacteria. So, in addition to discouraging pathogenic bacteria, MOS also promotes the growth of beneficial microbes such as *lactobacillus*.

MOS stimulates the immune system (Bland et al., 2004) and encourages the growth of intestinal villi, showing improved digestion and absorption of nutrients in various animal studies (Newman, 1994; Davis et al., 2000). MOS also enhances the immune system by raising the levels of plasma and colostral IgG and bile IgA antibodies. Passive transfer of immunity within the first 24 hours of the foal's life is crucial for protection against pathogens, which may otherwise result in diarrhea, sepsis, and even death.

Freedom Health uses MOS extracted from dried yeast.

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