An investigation into the efficacy of a commercially available gastric supplement for the treatment and prevention of Equine Gastric Ulcer Syndrome (EGUS)

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TAKE HOME MESSAGE

Equine Gastric Ulcer Syndrome (EGUS) has been found to be widely prevalent in both racing, and non-racing horses (Murray *et al*., 1989; Hartmann and Frankeny, 2003; Nieto *et al*., 2004; Chameroy *et al*., 2006). Traditional treatments often necessitate drug threrapy (Andrews *et al*., 1999), which may be expensive, and competition regulations could inhibit their use. GNF™ is a commercially available nutritional supplement, intended for daily feeding to horses with gastric disturbances. This trial investigated the efficacy of the product in the treatment of EGUS and found that horses supplemented with GNF™ for six weeks showed significant ($P<0.05$) reduction in overall ulcer score. It can therefore be concluded that GNF ™ can have effective results at reducing the severity of EGUS in affected horses.

INTRODUCTION

With the development of sophisticated methods of gastroscopy in recent years, Equine Gastric Ulcer Syndrome (EGUS) has become widely diagnosed in many animals (Hartmann and Frankeny, 2003; Nieto *et al*., 2004; Chameroy *et al*., 2006). It has been suggested that prevalence of the condition amongst racing Thoroughbreds may be as high as 90% (Murray *et al*., 1989), with gastric lesions being identified in 100% of racing animals in some instances (Murray *et al*., 1996). In non-racing horses, 51% of animals showing signs of gastric disturbance were found to be effected, with a further 37% of apparently healthy horses displaying significant numbers of lesions to be classed as suffering from EGUS (Bullimore *et al*., 2001). Clinical signs of the disease include weight loss, diarrhoea, decreased appetite, behavioural changes, decreased performance and colic (Murray *et al*., 1989; Murray *et al*., 1996; McClure *et al*., 1999; Vatistas et al., 1999; Bullimore *et al*., 2001; Nieto *et al*., 2004).

Purported reasons for the development of EGUS are wide ranging. Bullimore *et al*., (2001) suggest that ulceration arises from imbalances between defensive mechanisms and aggressive factors within the stomach. It is often assumed that excess acid and pepsin secretion in the glandular region of the stomach may be to blame. However, work in human sufferers of gastric ulceration have shown many patients to display near normal acid secretion (Grossman *et al*., 1963). It is therefore highlighted that defensive mechanisms within the stomach are just as vital in the prevention of ulceration. In the glandular region of the stomach, a mucus layer is secreted to protect against autodigestion, bacterial infection etc (Bullimore *et al*., 2001). It has been found that bicarbonate ions are secreted into the mucus allowing surface pH to be maintained near neutral, even when luminal pH is below 2 (Quigley and Turnberg, 1987). Mucus also contains the glycoprotein mucin. It is postulated that abnormal variations and molecular characteristics of mucins can compromise permeability of mucus gels, and therefore mucosal defence (Bullimore *et al*., 2001). Indeed, in human patients, gastric ulceration has been associated with abnormal mucin gene expression and glycosylation (Jass and Roberton, 1994; Filipe and Ramachandra, 1995).

Although it is acknowledged that the majority of EGUS lesions are found to be present in the non-glandular region of the equine stomach, it has recently been noted that a gene homologous to the human $MUC5_{AC}$ is expressed within the equine stomach in both glandular and non-glandular regions (Bullimore et al., 2001). $MUC5_{AC}$ is responsible for the production and expression of neutral mucins, and its presence in both regions of the stomach suggest some mucosal defence in the proximal stomach areas. Therefore, abnormal production of the gene may lead to reduced defence, as highlighted in humans (Bullimore *et al*., 2001). Other causes of ulceration are thought to be due to excessive acid build up (Jones 2002), which could lead to unnatural movement of acid in the non-glandular regions. This may be due to mechanical blockage of the stomach. However, this situation may be compounded in meal-fed horses given restricted access to forage, as stomach secretions are continuous, even when the stomach is empty (Frape, 1998). Furthermore, restricted forage intake is also noted to reduce salivary bicarbonate production, and thus reduce the overall buffering capacity within the proximal end of the stomach (Frape, 1998).

Treatment of EGUS is primarily with pharmacological agents that either act as H2 blockers or as acid pump inhibitors (Andrews *et al*., 1999). Nutritional supplements that have proven their efficacy in scientific trials could potentially be used as adjuncts to veterinary therapy following an initial course of drug treatment, or during periods were conventional drug treatment must be

withheld in order to avoid contravening doping regulations. However, it is the prevention of this disease, through management and possible supplementation of gastric treatments, which horse owners could use to ultimately reduce the high prevalence of EGUS.

The aim of this study was to investigate the efficacy of a commercially available gastric supplement, purported to increase mucin production and combine with natural bicarbonate production to produce defensive gels within the stomach.

MATERIALS AND METHODS

Animal Management

26 National Hunt Thoroughbred Racehorses were used in the study. All were aged between 4 and 10 years, and all resided on the same yard. All horses were maintained on their original diet, and all horses remained in their normal training routine. Horses were housed in stables, and were each turned out to grass for 1 hour per day. No additional supplements or conflicting medical treatments were given throughout the duration of the trial.

Animal Recruitment to the Trial

All animals used in the trial were routinely scoped for veterinary purposes. All horses recruited to the trial were to be scoped regardless of the trial, at the request of the trainer. Horses were initially scoped and divided into three categories depending on their ulcer score; Clear (ulcer score 0), n = 5, Mild to Moderate (ulcer score 1-2), n = 14 and Severe ulceration (ulcer score 3-4), n = 7, within which horses were further divided into supplemented (n = 14) and non-supplemented (n = 12) groups. Each group (treatment and control), were blocked to allow equal numbers of each ulcer score to be allocated to either treatment or control. Blocked animals were then assigned to treatments groups randomly. See table 1.

Horse Number	Ulcer score	Treatment (T) or Control (C)	Horse Number	Ulcer score	Treatment (T) or Control (C)
1	0	T	14	2	T
2	0	C	15	2	C
3	0	T	16	2	T
4	0	T	17	2	C
5	0	C	18	2	C
6	1	C	19	2	T
7	1	C	20	3	T
8	1	T	21	3	C
9	1	T	22	3	T
10	1	T	23	3	T
11	1	C	24	4	C
12	1	T	25	4	T
13	1	C	26	4	C

Table 1; Assignment of horses to treatments. Total numbers in each group were: Clear – Treatment, n = 3, Control, n = 2; Mild to Moderate – Treatment, n = 7, Control, n = 7; Severe – Treatment, n = 4, Control, n = 3.

GASTROSCOPY

Gastroscopic examination was performed after a fasting period of 20 hours and water was withheld for 4 hours prior to scoping. The examination was preformed at the request of the owner, by a registered veterinary practitioner. Examination was carried out using a video Med – V.10.300, CCD Cam 3 endoscope with Xenon XL – M180 light source. The scope measures in at 3 meters in length, with an external diameter of 9.8 mm. Each individual horse's gastroscopy was recorded on to a DVD for later consultation. A panel of veterinarians scored each horse and an average score was then given, the scoring system used is outlined in Table 2.

Horses were supplemented for a period of 6 weeks. All horses used in the trial were due to be re-scoped as part of the normal management after this time, therefore the trial was restricted to this length so as not to subject animals to unnecessary endoscoping procedures. Ulceration was then assessed as before. Nine horses were removed from the trial due to unrelated reasons that resulted in the cessation of training, this resulted in overall group numbers being – treatment n = 11 and control n = 6.

Score	Description
0	Epithelium is intact throughout; no hyperemia, no hyperkeratosis- normal
1	Mucosa is intact but there are areas of hyperemia and/or hyperkeratosis (thickening)
2	Small, single or multi-focal erosions or ulcers
3	Large, single or multi-focal ulcers, or extensive erosions/superficial lesions
4	Extensive ulcers, with areas of deep submucosal penetration

Table 2; Ulcer Scoring System (as proposed by EGUS Council)

SUPPLEMENTATION

The commercially available supplement, GNF™ was administered to treated horses at recommended levels of 100g/day, split between three feeds, for a period of 6 weeks. GNF™ is marketed as a gastric supplement intended for daily feeding to horses prone to gastric disturbances. It is purported that GNF™ will assist in maintaining optimum gut health and function, allowing maximum utilization of feed.

Compositional Analysis of Supplement	**Per 100g**
Calcium Carbonate	20,000 mg
Magnesium Hydroxide	10,000 mg
Seaweed Extract (from Laminaria Hyperborea)	10,000 mg
Fructo-oligosaccharides	10,000 mg
Glutamine	3,800 mg
Threonine	4,720 mg
Excipients and Binders (Full Fat Soya, Kaolin)	41,480 mg

JUSTIFICATION FOR INGREDIENT INCLUSION

Fructo-oligosaccharides (FOS) have recently been classified as prebiotics (Mikkelsen and Jensen, 2004); substances that are recognised to stimulate growth of desirable bacteria (Kapiki *et al*., 2007), which can result in a positive symbiotic relationship between bacteria and host (Gibson and Roberfroid, 1995). Due to the formation of ß-linkages in the monomer chain, FOS are categorised as non-digestible oligosaccharides (NDOs), as such linkages cannot be hydrolysed by endogenous enzymes (Burvall *et al*., 1979; Oku *et al*., 1984). As a consequence, FOS can remain available as substrates for microbial populations to utilise (Houdijk *et al*., 1998), and thus promote increased intestinal efficiency (Mikkelsen and Jensen, 2004).

Glutamine is implicated in the synthesis of proteins, as a fuel reserve for dividing cells and lymphocytes, (Krebs *et al*., 1980), and as a mediator in the development of intestinal epithelial cells (Windmueller and Spaeth, 1980; Wu *et al*., 1995). Glutamine supplementation has proven to increase intestinal performance (Yan and Qiu-Zhou, 2006), and has been found to decrease over-expression of pro-inflammatory genes, thus leading to a reduction in intestinal damage of rats receiving acetic acid supplementation (Fillmann *et al*., 2007). Glutamine has also been shown to be an essential requirement of extracellular fluid which is involved in the regulation of intentional cell volume changes, which occur as a result of cellular regulatory pathways (Ernest and Sontheimer, 2007).

Threonine is an essential amino acid and studies have shown that restriction of this nutrient may limit intestinal mucin synthesis and reduce gut barrier function (Hamard *et al*., 2007; Faure *et al*., 2005).

Laminaria hyperborea is a brown kelp or seaweed that has been found to be extremely palatable and provide increased digestible energy sources for sheep kept on the Orkney island of North Ronaldsay (Hansen *et al*., 2003). L. hyperborea contains higher amounts of vitamins, minerals and proteins, when compared to conventional vegetable sources (*ibid*.).

GNF contains both **calcium and magnesium** which are recognised as alkaline providers, and have been shown to increase intestinal mucosal integrity (Wang, 2000).

RESULTS

73% of supplemented horses showed an overall decrease in ulcer severity across all categories. This is in comparison to 33% of control horses showing an increase in severity, and a further 33% of control horses eliciting no change in ulcer score.

The data was tested for normality using the Kolomorgorov-Smirnov Test and found to be significant ($P<0.05$). It was therefore assumed that the data was not normally disturbed, thus a non-parametric test was used. Data was statistically analysed in SPSS using a two tailed Wilcoxon test, which allows unequal group sizes to be analysed. Overall scores (regardless of category) showed a significant reduction over the trial in supplemented horses, compared to control horses ($p<0.05$) (See figure 1). Statistical analysis on individual groups was not possible due to resultant low numbers in each, although supplemented horses showed a trend towards reduced ulcer scores.

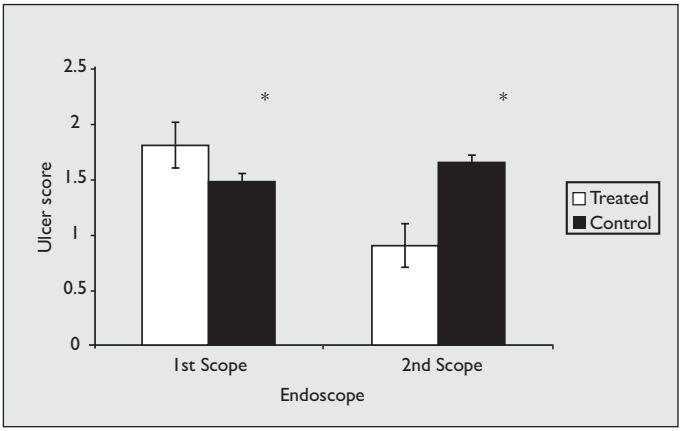

*Figure 1. Differences in ulcer score between the first and second gastroscopy exams, in both supplemented and control groups. * Indicates significant differences between the two groups ($P<0.05$).*

The average ulcer score for the supplemented group decreased from 1.82 to 0.91, whilst the average score for the control group increased from 1.5 to 1.66.

CONCLUSION

This study has proven the effectiveness of GNF™ , as a nutritional adjunct in the management of equine gastric ulceration. A significant difference ($P<0.05$) in ulceration score was recorded after 6 weeks of supplementation, with the treated group showing significant improvement in comparison to the control group.

Due to the exceptionally high prevalence of EGUS in the thoroughbred racehorse sector and the limited availability of clinically proven nutritional feed supplements on the market, the results of this research will provide the industry with an effective nutritional tool in the management of EGUS; in conjunction, where appropriate with proton pump inhibitors such as omeprazole and H2 blockers (e.g. ranitidine, cimetidine).

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