

Equine joint supplements

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In the Oxford online dictionary a supplement is defined as “a substance taken to remedy the deficiencies in a person’s diet”. Substituting horse into that definition it is striking that, when dietary deficiencies in horses are rarely identified in equine clinical practice, an internet search for “supplement” and “horse” yields more than 26 million hits.



Figure 1. The equine nutraceutical market is huge and is dominated by products designed to maintain healthy joints and soundness.

Many of us consider supplements are administered in the belief they may confer health benefits in horses that do not have a dietary deficiency per se when the term nutraceutical might be more appropriate.

Nutraceutical, that is, “non-drug substances produced in a purified or extracted form and administered orally to provide agents required for normal body structure and function with the intent of improving the health and well-being of animals”¹ or, more succinctly, “a food containing health-giving additives” (Oxford online dictionary) might be more appropriate.

Better still, “natural care product” clearly distinguishes these products from pharmaceuticals, since to claim a medicinal benefit for products that have not undergone a licensing process and do not

have a veterinary marketing authorisation would be illegal.

The UK equine nutraceutical market is immense. There are approximately 950,000 horses in the UK, with owners spending around £35 million on nutraceutical products each year (British Equestrian Trade Association data; **Figure 1**).

This figure is depressing as it dwarfs the amount spent on licensed veterinary products. It could be argued there is a financial incentive for manufacturers of equine “health” products not to demonstrate their products are efficacious as they would then be compelled to apply for a marketing authorisation and, in so doing, lose the ability to advertise their products to the horse-owning public.

The range of equine nutraceuticals is bewildering and commenting on their relative merits is impossible when many do not provide an accurate indication of their constituents. Many owners and trainers use nutraceuticals independent of veterinary advice and without any knowledge about the efficacy, safety and even constituents of what they are using. As vets, we are often asked to either recommend a particular product or commend a product the owner has found and are expected to have an understanding of the quality, efficacy, tolerance and safety of individual nutraceuticals when all too frequently these are not known (**Figure 2**).



Figure 2. Frequently owners expect us to be able to comment on the merits of various nutraceutical products and many practices now stock their own-brand products.

In addition to concerns over efficacy, it has been documented that when manufacturers make a claim regarding the structure or function of a product the so-called “guaranteed analysis” is variable in its accuracy. In a study of five equine glucosamine (GLN), five chondroitin sulphate (CS) and one combination product the actual combination of each component varied between 22.5% and 155.7% of the label claim². A second study looked at actual GLN content of 23 equine oral joint

supplements and found a range for GLN content of 0% to 221% of label claims. Out of 23 products, 9 contained less GLN than was claimed and 4 less than 30% of label claims³. Those compounds that state they are a “complex”, “formula”, or “blend” of ingredients without specific weights of components detailed are likely to be the most variable.

Many clients seem to think the words “natural” and “safe” are synonymous, but this clearly is not the case. The safety of nutraceuticals is generally assumed although rarely tested. Some manufacturers comply with voluntary schemes to ensure the safety of their products, but many do not.

Nutraceutical products have resulted in horses testing positive for banned substances at competition, prompting the Fédération Equestre Internationale to issue a warning of the risks of using supplements and herbal substances in horses competing under its rules.

Calling up the lists of “most popular” on the websites of equestrian retailers demonstrates how the equine nutraceutical market is dominated by products aimed at joint disease and “soundness”. On one site, all of the top 10 products were either products for “maintaining healthy joints” or were “natural” alternatives to NSAIDs.

Nutraceuticals have traditionally been used in joint disease in the hope they provide an excess of precursors for cartilage matrix to favour matrix synthesis and repair of articular cartilage⁴. Some products may also help to decrease articular cartilage degradation by decreasing the production of inflammatory mediators, degradative enzymes and free radicals.

The actual mechanism of action for most compounds sold for the maintenance of soundness is not known or is unproven in the horse. Observational studies, anecdotal reports and favourable testimonials do not provide proof of efficacy. The majority of nutraceutical products used in the treatment of joint disease and lameness contain one or a combination of the following ingredients.

Glucosamine

Three commercially available forms of exogenous GLN are available: hydrochloride (HCl), sulphate and N-Acetyl-D-glucosamine (NADG). The HCl and sulphate forms inhibit cartilage degeneration more consistently than the NADG form⁵. Glucosamine HCl is the most stable form and is twice as bioavailable as the alternatives. In controlled blind studies, those with positive outcomes used the HCl form.

Glucosamine is a small, water-soluble molecule and its bioavailability is reported to range from 2.5% to 5.9% in the horse⁶. There is good distribution of GLN to the cartilage with levels in cartilage exceeding those in plasma⁷. The actual effects of GLN may lie in its effects on non-articular tissues as it does not readily diffuse into synovial fluid from plasma and thus accumulation in articular cartilage may be limited⁸.

Glucosamine has a number of potential modes of action:

- It is required for the synthesis of glycoproteins and glycosaminoglycans (GAG).
- It reduces prostaglandin E2 (PGE2) levels and cyclo-oxygenase-2 expression⁹ and therefore has anti-inflammatory potential
- It stimulates proteoglycan and GAG synthesis while decreasing proteoglycan degradation and may therefore preserve cartilage¹⁰.
- It has an anti-catabolic effect in vitro.

Controlled studies in horses are lacking; however, two reports of young horses in training found no significant differences in serum markers in response to the administration of GLN^{11,12}.

Chondroitin sulphate

CS is derived from shark and bovine cartilage. It is difficult to synthesise or extract and, being more expensive than other ingredients, is rarely found as a sole therapy¹. Chondroitin sulphate is thought to enzymatically degrade as opposed to directly absorb from the intestinal tract, with studies in horses demonstrating good bioavailability (32%) of the low molecular weight form⁶.

In humans, absorption is rapid and cartilage and synovial fluid concentrations exceed plasma concentrations, resulting in accumulation with repeat dosing. This may explain the reported delay in treatment effect of two to four months and prolonged benefits after treatment has stopped¹³. Chondroitin sulphate may have anti-inflammatory effects through inhibition of inducible nitric oxide synthase and matrix metalloproteinase production and increased synthesis of prostaglandins and GAGs¹⁴.

GLN and CS combinations

Many products combine GLN and CS. Cosequin (Protexin) is one of the better known formulations containing GLN HCl, CS, manganese and ascorbate (vitamin C). Vitamin C is a free radical scavenger that may provide anti-arthritis effects by protecting chondrocytes from oxidative damage¹.

This combination has been shown to improve collagen synthesis in tenocytes and ligament cells, as well as having synergistic effects on articular cartilage. Improved lameness scores, responses to flexion and stride length have all been demonstrated following oral administration¹⁵ and horses with lameness attributable to navicular bone remodelling showed significant improvements in soundness compared with controls receiving a placebo¹⁶.

However, one of these studies¹⁶ only contained 14 horses, and the other¹⁵ lacked a placebo group and was neither randomised nor blinded. Safety of the product has been established in a study in which mares were administered five times the recommended dose for 35 days without detrimental

effects¹⁷. A recent controlled study evaluating the response of 24 geriatric horses to a combination product containing GLN, CS and methylsulfonylmethane (MSM) failed to demonstrate a beneficial effect of treatment on carpal flexion, range of tarsal motion and stride length compared to controls after three months of treatment¹⁸.

Given differences in results between studies and the products themselves it should not be assumed these findings can be extrapolated to all similar combination products.

MSM

MSM is a normal oxidative metabolite product of industrial grade dimethyl sulfoxide (DMSO) that is also found naturally in fruit, alfalfa and maize. It is soluble in water, but little is known of its pharmacokinetic properties¹.

MSM has been shown to prevent inflammatory joint disease in mice¹ and is used widely for the management of musculoskeletal disease in horses. However, to the authors' knowledge no controlled or clinical studies support the use of MSM in equine orthopaedic disease.

Avocado-soybean unsaponifiables

Unsaponifiable oil extracted from avocado and soybeans has been investigated as a treatment for arthritis in humans for more than a decade and more recently has also been used in horses. When compared to a placebo group, treated horses showed a reduction of cartilage erosion and synovial haemorrhage and benefits were superior to those of hyaluronic acid and polysulfated GAGs. However, there was no improvement in lameness¹⁹.

Oral hyaluronan gel



Figure 3. Nutraceutical products are typically administered orally, but intra-articular versions are also popular.

Hyaluronic acid has been used for 40 years as an intra-articular (**Figure 3**) and intravenous preparation in the belief it is disease modifying and reduces lameness associated with joint disease.

As an integral component of synovial fluid and articular cartilage, hyaluronan contributes to the viscoelastic properties of synovial fluid and lubrication of the synovial membrane and articular cartilage. An oral form of hyaluronan is commonly marketed as a joint supplement for use in young horses to help prevent osteochondrosis dissecans (OCD) and in older horses to increase viscoelasticity of synovial fluid.

In one study of effused tarsocrural joints with OCD fragments, daily administration of 100mg hyaluronan gel orally postoperatively for 30 days resulted in significant reductions in effusion scores compared to placebo controls²⁰.

However, a further double-blinded, placebo-controlled study failed to demonstrate significant differences in synovial effusion and inflammatory mediators in tarsocrural joints affected with OCD²¹. Bioavailability of the product in horses is not known and many formulations are marketed with little information on their precise contents.

Green-lipped mussel extract

The New Zealand green-lipped mussel (*Perna canaliculus*) has been used in humans for many years as an important source of nutrients for healthy joint metabolism.

The mussel contains a combination of essential fatty acids and other nutrients including GLN and CS. In addition to the potential benefits of GLN and CS discussed previously some of the essential fatty acids have been demonstrated to have a measurable effect on enzymes involved in joint inflammation²².

Epiitalis

Epiitalis is a patented plant extract; a simulated digest of *Biota orientalis*. The product has been tested both in vivo and in vitro, with double-blinded, placebo-controlled trials and fared favourably in a review of glucosamine-based nutraceuticals²³.

Horses given the product in feed showed a reduction in synovial fluid PGE2 in both experimentally induced (IL-1) arthritis and following carpal or fetlock chip removal. There was also a reduction in GAG (a cartilage breakdown product) in horses^{24,25}. It is now the “joint supplement” of choice in Australasia, is rapidly gaining a market share after introduction in Kentucky and is about to be made available in the UK.

Practice-branded products

Increasingly, equine practices carry own-branded nutraceutical products to ensure their clients receive reputable products. As retailers of such products we need to be careful not to present them as a veterinary medicinal product and by so doing breach the legally binding veterinary medicine regulations (<https://www.gov.uk/guidance/legal-controls-on-veterinary-medicines>). Any product that is medicinal by presentation must have a marketing authorisation issued either by the secretary of state or the European Medicines Agency.

A product is considered medicinal if the averagely well-informed consumer gains the impression the product treats, prevents or controls a disease, or the product restores, corrects or modifies physiological functions by exerting a pharmacological, immunological or metabolic action. We should therefore refrain from making any such claims for nutraceutical products.

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