

Literature Review-Joint Supplements (Nutraceuticals)

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Introduction

The health of our joints affects every aspect of our lives. The pain and loss of mobility can be crippling. The same applies to the animals in our lives. Our horses and dogs are seriously affected by joint disease as well. So it is no surprise that joint health is a popular area of research – both in human and veterinary medicine. The use of nutritional supplements (called “nutraceuticals”) has been popular for over a decade, but the scientific basis for their use has been somewhat limited. Not surprisingly pharmaceutical prescription “drug” treatments have been given the most attention.

Nutraceutical versus Prescription Drug – Which Is Better?

I find it helpful to understand the practical differences between drugs (defined as substances developed, patented, and marketed by pharmaceutical companies – and evaluated by the FDA) as opposed to nutraceuticals (substances derived from foods or other relatively unprocessed natural materials). While many of the policies and profits of pharmaceutical companies are questionable, the reality is that any substance considered to be a “nutraceutical” by the United States FDA cannot be patented and does not have to be tested by the FDA (is “unregulated”). This has enormous consequences for us, some good and some bad! No patent means that ANY ONE CAN MAKE AND SELL A NUTRACEUTICAL. For example, if a pharmaceutical company decided to test glucosamine to see if it really works for osteoarthritis, they could invest over 500 million dollars. This includes the human testing to prove it works and is safe. But once they have done this – because glucosamine is an unregulated nutraceutical - anyone can manufacture and sell glucosamine. And since potential competitors didn't have to spend 500 million for testing and development, they can sell it for a lot less than the pharmaceutical company. So it makes no sense for a pharmaceutical company to test and sell nutraceutical, at least in the United States where patent laws do not protect their sale. Consequently, US companies are going to limit themselves to development of drugs (anything not a food) so eventually a patent can be issued to the company who did the development and testing (and spend 500 million dollars). In practical financial terms, this means they are the only company allowed to sell this particular drug for several years – so they can try to pay for the cost of development, and eventually make a profit. (The patent situation is very different in many other countries. In countries like Germany, patents may be issued for nutraceuticals, so it becomes financially feasible to sponsor nutraceutical studies. This is the case with glucosamine sulfate which has been extensively studied by Rotta Pharmaceutical in Italy, and their product is sold exclusively by them.) Fortunately, there are some not-for-profit agencies in the US which will sponsor nutraceutical research. (The National Institutes of Health has recently conducted a study on glucosamine for joint health). Some non-profit private foundation or academic institutions sponsor relevant research as well – but this is a small portion of the total research effort).

Consequently, NSAIDs (Non Steroidal Anti-Inflammatory Drugs) like aspirin, Ibuprofen, Naproxen, Diclofenac (and more recently Celebrex, Bextra, and Vioxx), which can be patented, have been extensively studied and brought to market. Many have been approved for use in dogs and horses as well as humans. While the NSAIDs as a group are quite effective for relief of symptoms (pain and swelling), they do not seem to improve the joint structure of cartilage, or slow the progression of disease. Of more concern is that they may have significant side effects (Vioxx was pulled from the market because of concern about heart damage). The good news for us as animal owners is that nutraceuticals are more easily and cheaply available than prescription drugs (anyone can sell them, no prescription and no FDA regulatory requirements). The bad news is that there is no requirement for safety or effectiveness testing. Unfortunately some nutraceutical companies are just as interested in profit as anyone else, and take advantage of the lack of regulation. Such companies shamelessly take advantage of fads and misinformation.

“Natural” is Not Always Good

The best example is the use and abuse of the term “NATURAL.” Many nutraceutical companies (also food and cosmetic manufacturers) describe their product as “natural” – implying that this makes their product somehow safe, of high quality, and is somehow “better” than “synthetic.” This is nonsense of course. Consider, for example, thyroid medication for people with low thyroid hormone output from their own glands, (or who have had their entire thyroid gland removed surgically because of cancer). Replacement thyroid hormone is available in two basic forms: “Synthroid” is identical to the hormone made by your own human gland (but produced “synthetically” in the laboratory). The other kind is “Armour” thyroid. This is “natural” since it comes from pigs, but not only is it slightly

different from human hormone in its molecular structure, but it is manufactured from highly stressed slaughterhouse pigs, and different batches have different strengths. Which would you prefer? It is clearly simplistic to believe that natural is better. Obviously most things from nature are not safe. There are relatively few plants that humans can safely eat (look at any forest or grassland and count the number of plants you see – then consider how many are edible. In fact, most plants are at quite indigestible and many highly toxic to humans. The most potent poisons we know are “natural” (foxglove, oleander, mercury, lead, arsenic, etc).

What You Should Know About "Studies"

The following section is a summary of some of the available research on joint nutraceuticals for horses and humans. Some of the studies are considered very well designed from a scientific perspective.

They are called comparative, placebo-controlled studies.. That is, they usually have two (or more) groups or subjects (peoples or horses or dogs or...). One group (experimental group) is given the substance being tested. The other group (control group) takes a placebo (that is, a substance that looks and tastes the same as the test substance, but is missing the active ingredient). Then, the study tries to keep everything else about the two groups the same (“controlled”). That is, the number of geldings or mares identical in each group, they should also be the same ages, receive the same feed, shelter, exercise, have the same health history, and identical general care and attention. This is difficult enough to do with humans, who can cooperate, but very difficult to do with horses. As a result, there are relatively few such comparative, controlled studies.

Another study design may be simply what a called a longitudinal study. Here, horses with stable arthritis are given a nutraceutical for some months and see if they improve, then it is stopped to see if the symptoms come back. This can be helpful, but the problem is they might have improved anyway – because of weather changes, or simply because joint problems can come and go without apparent explanation.

Expert Opinion Can Be Useful

Even more variable is the opinion of “experts” (just like this article!). Just having a degree (DVM, MD, PHD,) doesn't really tell you anything about that expert's actual expertise. Most experts automatically have some kind of bias (we have done a study and defend our result, we “want” something to work, we are selling a product, or hired by a company which is selling a product, or we have an academic reputation to support).

Personal Experience Counts

What about our own personal experience? We call this “anecdotal” evidence. What if we experience improvements in our own health when we take a new nutraceutical or drug or food? What if we see big improvements in our horses or dogs? What if our vet or personal physician believes a particular drug or nutraceutical has helped many of her/his patients? This is important information, and it too can be valid. But remember that there could be other reasons we or our horses felt better. Again, maybe a change in weather, feed, rest, or rehab exercises, physical therapy, fitness training, or just more TLC and general attention could be helping the joint pain. Or maybe the arthritic attack just improved spontaneously.

You Be The Judge

When you are evaluating use of nutraceuticals for yourself or your horses (or use of drugs or even foods) remember to assess and question the quality of the evidence:

1. Is it anecdotal evidence?
2. If it is an expert opinion, does the expert back up her/his opinion by referring to reliable studies. What is the expert's bias?
3. Are there controlled, comparative studies, published and evaluated by other experts?
4. If the studies are published, how are they published and by whom? Just being on the internet is obviously no guarantee of reliability. If information is published in a book or magazine, assess the reliability of the publication. Some books and articles are published by the author himself, and have not been evaluated by anyone else. Some magazines simply publish ideas which are interesting and entertaining, but no real basis in fact – just one reporters opinion.. Many magazines will publish an article for you, if you buy advertising space in their magazine. So-called “peer-reviewed” publications are generally the most reliable. In human health, JAMA (Journal of the American Medical Association) and NEJM (New England Journal of Medicine) are good examples, but someone's “Heath Newsletter” is probably just the opinion of one group within a University or Hospital or Veterinary College, or simply an individual who want to sell their Newsletter to you. In veterinary medicine, publications like The Veterinary Journal are peer reviewed. Equus or Practical Horseman are not. There are hundreds of others.

Is the Supplement Pure? Is the Dose Correct?

Be sure the Nutraceutical supplement you buy is pure and that it has enough in it to actually do some good. Recommended doses should be based on the best available studies which showed a positive effect. Many supplements add trivial amounts of things like Vitamin C , Vitamin E, glucosamine, MSM and so forth.

Is the Supplement Working?

Be patient and be willing to try something for at least 8 to 12 weeks or longer, before deciding if it is helping. Try to come up with a way to measure progress with careful observation of degree of obvious lameness, smoothness of gaits (preferably on both hard and soft surfaces), informal (or formal veterinary) flex test, voluntary movement at turnout and so forth.

Why Use the EasyGait Formula?

We have chosen a simple combination of 3 ingredients which have reasonable scientific basis for use, and are very safe. Our goal is to make this available to the average horse owner at the best possible cost. We will attempt to keep up with the latest scientific findings in these areas, and will modify our supplement accordingly. We also solicit your input for information we have missed, and would definitely like to learn about your experience with nutritional supplements for your horses.

Research and Expert Opinion

1. GLUCOSAMINE

There is more information available about glucosamine (G) than any other supplement used for joint health. This is primarily because it seems to be effective for human use (1), as well as for animals (primarily horses and dogs) (2,3). Arthritis is a major illness in people, and pharmaceutical companies compete intensely for market share in this area. As a result, we have many "arthritis drugs" beginning with aspirin, and now with literally dozens of different medications (Ibuprofen, Naprosyn, Celebrex, to name just a few). Glucosamine may have some of the same anti-inflammatory and pain relieving effects of NSAIDS, with the added benefit of fewer side effects, and it may actually help restore the integrity of cartilage in the joints, (which NSAIDS do not appear to be able to accomplish).

HOW DOES IT WORK?

There is considerable confusion and debate about this. Originally, it was suggested that the glucosamine molecule may actually be incorporated into the cartilage structure itself – making it stronger. More recent studies suggest that the actual amounts of glucosamine absorbed into the blood and joint fluid may be too low to actually form building blocks in cartilage, but may stimulate growth of cartilage in other ways. In addition glucosamine may activate (or inhibit) other chemical reactions which slow the breakdown of cartilage (4,5,6,7,8). (Cartilage, like other tissues in the body, is always simultaneously growing and breaking down. It is the balance between the two that is important. For example, If bone growth is faster than break down, then bones will heal and grow stronger. But if breakdown is faster than growth, then bones get thinner and osteoporosis results.) Glucosamine may also work to reduce production of substances which cause inflammation in tissues. (9)

WHY GLUCOSAMINE SULFATE?

The glucosamine molecule is available commercially in several forms. The usual type found in commercial supplements is glucosamine attached to sulfate (GS) or to hydrochloric acid (GHCL). Most of the many human studies on glucosamine have been done with GS. Relatively few studies have been done with GHCL. Many have been sponsored by Rotta, an Italian company who has brought GS to market and therefore to the attention of the nutraceutical and medical communities. The sulfate part of GS contains a sulfur atom, and sulfur is an important part of the chemical structure of cartilage. Many experts feel that the sulfur is just as important as the glucosamine, and together they work effectively (1,10). (Note – sulfur may also be provided by MSM or chondroitin sulfate (CS) in some supplements). Since sulfate weighs more than HCL (hydrochloric acid), the same weight of GS has less G than in GHCL. On the other hand, it contains sulfur, (There is no sulfur in GHCL). A recent review of all human G studies concluded that some studies showed benefit for joint disease, and other studies did not show any benefit. Interestingly, The effective studies used GS, while most of those with no benefit used GHCL. A recent study conducted by the National Institutes of Health concluded that moderate or minimal benefit resulted from use of GHCL combined with CS. Interestingly, either one alone had no benefit. This makes sense if you realized that you need both the glucosamine and the sulfur together to have maximal benefit.

WHAT ELSE DO WE KNOW ABOUT GLUCOSAMINE SULFATE?

1. It is absorbed from the intestine into the bloodstream. It does move from the bloodstream into the joints in people and horses. Studies show that most of the G is absorbed from the gut and then quickly broken down and incorporated into various tissues, Only 2-3 % of the original dose stays in the form of the original G molecule in the blood and in the joints. By comparison, a larger % of CS is found in the bloodstream in unmodified form (11). But this doesn't necessarily mean that CS is more effective. There is evidence that G works by reducing cartilage breakdown, and that very small amounts are needed to achieve this effect (12). What is the evidence for this? It comes from cultures studies where horse joint cartilage is placed in the laboratory, and various amounts of G added to see what happens to the cartilage. If G is injected IV, then more may reach the joints in the original form (less breakdown via digestion in the gut and the liver). But it is potentially more expensive and requires frequent injection (which carries its own risks). It has also been suggested that G has some beneficial effect on intestinal tissues when it is given orally. G may also work by strengthening other tissues outside of the joints (tendons, ligaments, muscles) Accordingly, the actual amount of the unaltered molecule that stays in the bloodstream may not be particularly important. So we really can't say yet that injectable G is more effective than oral dosing.

2. GS has no known toxicity – is very safe. This has been confirmed repeatedly in horse and human studies. In a recent study on absorption, horses were given 10 times the usually dose, and still had no adverse effects (3,11, 13).

3. GS stays in the body for several hours and is quickly absorbed and metabolized by various tissues (Only about 10% is actually lost in the manure. All the rest is absorbed.) One study found higher amounts of GS in people who had been using G on a daily basis before entering the study (14). Daily dosing makes sense.

4. GS has been shown reduce pain and inflammation in many human studies (but not all) (1,15). There is much less work on horses. (See Section IV)

5. GS may actually help restore damaged cartilage. – that is, it may have long term preventive effects .and may actually provide long term protection for the joint. Most of this information comes from human studies. A recent study actually showed that the human knee joint might show significant repair after 3 years of GS use (16).

6. The optimal dose for humans is probably about 1500 mg daily. Doses for horses cover a wide range in commercial supplements. If one extrapolates from human doses to equine, based on body weight, then equivalent dose for horses is about 8 to10 gms daily. (8,000 to 10,000 mg).

II METHYLSULFONYLMETHANE (MSM)

In spite of its widespread use, MSM really hasn't been studied all that much. In humans, MSM has been evaluated mainly as a treatment for allergy - to help reduce inflammation. In theory, MSM (which is closely related to DMSO chemically) may reduce muscle pain and spasm. There is some evidence for joint protection in humans (17), but no controlled studies in horses. Because MSM has a high content of sulfur, it may help with cartilage structure (similar to the sulfur in GS). Toxicity and safety profile are good. In summary, MSM may have significant benefit for horses, even though the scientific evidence is scanty (3).

III VITAMIN C (CALCIUM ASCORBATE)

Vitamin C has been studied extensively – both in the laboratory and in human and animal studies. It is well know as an "antioxidant." This is a molecule that may inactivate harmful substances in the body called "free radicals" which can cause various types of cellular damage. Vitamin C is also commonly used as an antioxidant preservative in foods and many animal feeds – since it helps prevent deterioration. In humans, Vitamin C is used for treatment and/or prevention of various ailments – including the common cold. There continues to be considerable scientific controversy about some uses of Vitamin C since some studies showing benefit, others not. The dose is one of the critical factors, since many human clinical studies have used very low doses (less than 100 mg daily) even though many experts believe higher doses are necessary to show any benefit (2000 to 10000 mg daily). But it is generally agreed that vitamin C does support synthesis of collagen (important component of elastic and muscle tissues), will stimulate activity of certain white blood cells, and speed healing of wounds. It is clearly an antioxidant as well.

In horses, a few studies on racing thoroughbreds (18), endurance horses (19), and human athletes (20) show higher levels of vitamin C in the blood during exercise, which may prevent cellular damage. Vitamin C is also used as an effective treatment for recurrent airway obstruction in horses (also called "heaves") (21). This is very similar to asthma in humans. More importantly for our purposes, vitamin C may protect cartilage from degeneration. One long term (uncontrolled) study on lame horses showed improvement in 9 of 10 animals (22). Even in very high doses, vitamin C doesn't have any adverse effects. Doses should probably be at least several grams daily to be effective.

DOES THE INFORMATION FROM HUMAN STUDIES REALLY APPLY TO HORSES?

The simple answer is we don't know for sure, but a great deal of it could be relevant. Much that we have learned about nutrition, drug treatment, and disease has come from animal studies. So applying human information to horses makes sense – as long as one is cautious- particular about safety. Compared to human studies, there is less scientific information available from studies actually done on horses., but what is available is very promising.

STUDIES ON HORSES

Two important clinical studies in horses used glucosamine, chondroitin sulfate, and a small amount of vitamin C. for treatment of osteoarthritis or navicular disease (23,24). Within two weeks, horses with arthritis had a significant improvement in lameness scores; however, flexion tests and stride length did not change. Horses with navicular syndrome had significant improvement in lameness scores at eight weeks. This was the first randomized, double-blind placebo-controlled clinical trial in the horse.

Another important study was carried out by Dr, Hilary Clayton at University of Michigan. She conducted a double blind study comparing use of Cortaflex to placebo in working horses with some degree of stiffness and asymmetric gait. She used pressure plates for gait evaluation, and found some improvement in range of motion and smoothness of gait after only 2 weeks of supplement use. (Cortaflex contains precursors of glucosamine and chondroitin.) (25)

This is still a young field, and we will know much more ten years from now. In the meantime, using joint supplements for your horse seems to carry no real risk, and may have a great deal of benefit!

RECOMMENDED READING-MEDICAL AND VETERINARY LITERATURE

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