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ORAL JOINT SUPPLEMENTS: PANACEA OR EXPENSIVE FAD?

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Introduction

Athletic competition often requires horses to run, jump, turn, start, and stop, placing an enormous strain on the skeletal system. As such, a performance horse may fail to reach its athletic potential or a seasoned athlete may not stay at the top of its sport because of lameness. Injuries and diseases of the joints are common causes of lameness. Because joint problems can be a limiting factor in career longevity of athletic horses, care and maintenance of joints is a major concern among horsemen.

Joint health is an evolving science. Researchers are investigating many novel equine joint therapies. A relatively new approach to joint health is the use of oral joint supplements. Advertisements for joint supplements are in almost every horse-related periodical, and tack store shelves are lined with concoctions designed to improve joint health. Despite their prevalence in the market, much confusion exists regarding these products. The following is a brief summary of the information available on joint supplements.

Joint Supplements as Nutraceuticals

Joint supplements are loosely classified as nutraceuticals. The term "nutraceutical" combines the word "nutrient" (a nourishing food or food component) with "pharmaceutical" (a medical drug). The word nutraceutical has been used to describe a broad list of products sold under the premise of being a dietary supplement (i.e., a food), but for the expressed intent of treatment or prevention of disease. In the case of joint supplements, they are sold as dietary supplements with a twist. The claims (usually made by manufacturers) of their ability to aid in equine joint health provides the twist. A potential difference between a feed and a nutraceutical is that a nutraceutical is unlikely to have an established nutritive value. Feeds are required to have nutritive value and are accountable, via labeling, for these values. Another difference between a feed (food) and a nutraceutical is that feed is "generally recognized as safe (GRAS)." Nutraceuticals may contain substances that are "natural" but may not be generally recognized as safe. The primary stumbling block in adding the "active" compounds found in joint supplements into horse

feed is that these substances do not have a GRAS statement on file with feed regulatory agencies. Thus, inclusion of the joint supplement in the feed and listing its name on the feed tag are illegal due to the lack of established safety data.

The definition of nutraceutical includes the statements "for disease treatment and prevention" and "administered with the intent of improving the health and well-being of animals." When a dietary supplement, nutraceutical, or other feed is used for the treatment or prevention of disease, in essence it then becomes a drug. Drugs are subject to an approval process prior to marketing. To be approved, a drug must demonstrate safety and efficacy for its intended use. Drugs that are not properly approved are subject to regulatory action.

From this discussion, it seems joint supplements fall somewhere in between food and drug. They have many advantages over foods or drugs because they are not required to list ingredients and nutrient profiles as required by feeds, and in many cases are intended to treat or prevent disease without first undergoing proper drug approval. Determining if a product is a food, or is subject to regulation as a drug, is a function of the manufacturer's claims that establish intent.

The Goal of Joint Supplements

With vague label information, it is difficult to determine what the manufacturers of joint supplements intend as an exact function for their products. It is not difficult, however, to determine what is implied and expected by horse owners who buy the products. In most cases, joint supplements are fed to horses for one of two purposes. The first intended purpose is to heal the lame or to make chronically unsound horses sound. Unfortunately, horses can be lame for a number of reasons, and a single joint supplement could not possibly be successful in treating all causes of lameness. Even with other, more studied approaches to treating lameness, recovery is not expected in every case.

The second intended purpose consumers have for feeding oral joint supplements is to prevent joint problems from ever occurring. Unfortunately, many horse owners have seen the career of a talented horse cut short due to joint problems. These owners have since vowed to do "everything possible" to prevent the problem from occurring in other performance horses. Again, this expectation may be unrealistic due to the vast number of opportunities that athletic horses have to take a bad step and become injured. Do oral joint supplements work in horses? Some horse owners swear by them, while others do not see results. The unrealistic goals that both consumers and manufacturers have placed on joint supplements, horse to horse variability, and different underlying causes of lameness explain at least some of the differences of opinion regarding effectiveness of oral joint supplements. The key to understanding the efficacy of a joint supplement is to first comprehend the basics of joint anatomy and physiology. An understanding of the tissues involved in a joint and of normal joint function will provide rationale for many of the ingredients used in joint supplements.

The Equine Joint

A joint is the union of two bones, regardless of the location in the body. A joint allows controlled movement of bones relative to each other, thus allowing the skeleton to move. Joints found in the leg of a horse endure incredible pressure during movement. Normal horse movement begins with muscle contraction. Shortening of muscle fibers moves the bones via tendons that attach muscle to bone. Excellent descriptions of normal joint movement were written by Karen Briggs and published in The Horse (March, 1997 and November, 2000). The following is a summary of those descriptions taken with permission from The Horse.

In a healthy joint, the ends of the bones are coated with a thin layer of friction-reducing articular cartilage. They are also surrounded by a joint capsule with a tough outer layer (to connect the bones and protect the joint) and a permeable inner layer, or synovial membrane, which secretes synovial fluid and allows the passage of nutrients and other elements from the bloodstream. Synovial fluid, a slippery, viscous liquid that many researchers describe as being about the same consistency as egg whites, fills the joint capsule, nourishes the articular cartilage, and provides essential lubrication.

Synovial fluid is a nutrient-rich brew that contains proteins, enzymes, water, leukocytes, and a key ingredient, sodium hyaluronate, which is responsible for the fluid's elastoviscous qualities. Sodium hyaluronate (formerly known as hyaluronic acid) is a negatively-charged sugar chain, or glycosaminoglycan (GAG), which arranges itself in complicated coils, adapting to the pressure changes in the joint capsule as the horse moves. It assures the unhindered passage of metabolites to and from tissues throughout the joint, and also serves as a stabilizer and shock absorber for the structures that are undergoing continual, changing mechanical stresses.

Articular cartilage, the other main shock-absorbing component of a joint, is an efficient but flawed structure. Its structural framework is a web of collagen fibers, with cells called chondrocytes scattered along the matrix. Chondrocytes produce giant proteoglycan molecules that bind the GAGs. The GAGs in turn extract and loosely hold large amounts of positively-charged water molecules. When cartilage is damaged, there is a decrease in the number of GAGs; therefore, the cartilage holds less water.

Among the talents of cartilage, it conforms to the bone surfaces for a tight fit between weight-bearing bones; it spreads pressure evenly over a broad area; and it manages the water in its matrix, squeezing it out when the joint is under pressure, and drawing it back in when the joint is not under pressure. This in and out movement of the fluid transports nutrients throughout the cartilage. In a way, cartilage also acts like a sponge, conforming to loading demands by changing its shape and size, and regaining its original shape when the pressure is off. This "squeeze film lubrication" is the most important part of cartilage on cartilage

lubrication. This cartilage lubrication is much like hydroplaning – there is a thin coat of water between surfaces acting to decrease the coefficient of friction.

But here is the downside. Cartilage is one of the body's most primitive structures. It has no blood or nerve supply of its own, so cartilage has little or no ability to heal or repair itself. Only in rare cases when the cartilage is torn directly off the bone can healing take place (because the resulting space allows capillaries to break through and patch up the holes with fibrocartilage). Even then, the repair work is substandard and will not stand up to repeated stresses. As a result, although cartilage performs admirably under normal conditions, it only takes a 5-10% overload of work stresses to begin deteriorating.

Joint Damage

Lameness can result from damage to any of the tissues associated with the joint. If ligaments, tendons, or muscles are disrupted due to injury, instability of the joint can result. This ultimately results in a change in the normal range of motion of a joint and lameness. Likewise, disease of the supporting bone can lead to collapse of the joint surface and painful lameness. Damage to the articular cartilage such as breakdown of collagen and loss of proteoglycan result in weakened cartilage. This weakened cartilage develops cracks and holes and loses its smooth articulating surface, resulting in lameness. Similarly, damage to the synovial membrane and changes in the makeup of the joint fluid result in alternations in normal joint viscosity and still another reason for lameness. So what is the underlying reason for joint damage? The answer is quite simple – inflammation.

Inflammation is normally a protective mechanism initiated by the body in response to injury. It is often localized to a particular area of the body and begins as a result of injury to or destruction of body tissue. It is the initial response in a series of events that lead to the attempted repair of the injured tissue. Inflammation causes blood vessels to dilate and allows fluid and cells to leak out. The cells that are released into tissues during inflammation are primarily white blood cells. In turn white blood cells release a variety of chemicals and enzymes into the inflamed area. The inflammation response in a joint is a process designed to break down and remove injured or foreign material. The process of breaking down and removing the foreign bodies from the area changes the chemical makeup of the fluid in the joint, introducing excess fluids and a high concentration of destructive enzymes and prostaglandins into a closed area (the joint capsule). This destroys the lubricating GAGs. The synovial fluid begins to lose viscosity. The chondrocytes eventually suffer from a compromised nutrient supply and cannot keep up with repairs. The cartilage develops damaged areas, opening the bone ends to direct trauma. The bone responds with a defense that only causes further destruction; it lays down new bone to strengthen the surface (sclerosis) and extends its margins in the form of bone spurs. If left unchecked, this inflammation, known as arthritis, will totally destroy the joint.

Treatment Strategies

Many options exist for treating joint disease in horses. The major treatment goals are to reduce inflammation, to improve joint fluid, and to improve cartilage. Treatments to accomplish these goals generally fall into two categories, physical therapies and medical therapies. Physical therapies include rest, bandaging, application of heat, application of cold, and mild, controlled exercise to maintain range of motion. Forty years ago, medical therapies to treat joint disease were limited to liniments, blisters, sweats, poultices, application of DMSO (dimethyl sulfoxide, an anti-inflammatory), NSAIDs (nonsteroidal anti-inflammatory drugs such as phenylbutazone), and corticosteroids injected directly into the joint.

Treatment options for horses with joint disease began to change about 30 years ago when scientists first attempted to replace some of the natural constituents of joint fluid and/or cartilage, with the hope that the body could use those building blocks to restore normal joint function. The first product used was hyaluronate. Hyaluronate is a proteoglycan and an important component of joint fluid and joint cartilage. Hyaluronate can be injected directly into the joint, and more recently, a new form of the drug can be injected systemically. Hyaluronate is thought to increase the viscosity of synovial fluid, inhibit some of the damaging enzymes, and promote the synthesis of more sodium hyaluronate. Polysulfated glycosaminoglycan (PGAG) is another powerful class of drugs used for the treatment of joint disease. Remember that GAGs are negatively-charged molecules that bind and hold water. The water helps the articular cartilage manage the pressure of weight bearing. These drugs have been shown to be anti-inflammatory and to increase the production of the proteoglycan component of cartilage. PGAGs can be injected intra-articularly or intramuscularly to achieve positive treatment results.

Oral Joint Supplements – Proposed Mode of Action

About 10 to 15 years ago, supplement manufacturers combined many of the materials found in healthy joints into an oral supplement. The thinking process was quite simple: put the building blocks for a sound joint in a bucket, feed it to the horse, and let him absorb and utilize the materials to repair joint tissues. With this logic, treatment options went from intimidating needles to a harmless scoop of powder or pellets. The manufacturers of joint supplements typically include a number of ingredients that may have beneficial results. The average joint supplement will contain nutrients, derivatives of nutrients, and herbs.

In order for a joint supplement to achieve its desired effect in a living horse, several things need to happen. First, the substance must get absorbed across the gut. Second, the substance must get to the joint following absorption. Finally, if the substance gets to the joint, the body must utilize it for repair functions. Two

of the most common ingredients included in joint supplements are chondroitin sulfate and glucosamine.

With respect to chondroitin sulfate, absorption is debatable due to its large molecular weight (size). Chondroitin sulfate is typically obtained from bovine, whale, and shark cartilage. Several studies have characterized the intact absorption as low; however, more studies are under way that will use digestive data from horses. If chondroitin sulfate is absorbed and if chondroitin sulfate reaches the joint, what is the potential mode of action? As you may remember, articular cartilage consists of water, collagen, and proteoglycan. Chondroitin sulfate is the primary GAG that makes up the proteoglycans found in joint cartilage. It is known that joint injury and the ensuing inflammation cause a reduction in the amount of proteoglycan. Thus, chondroitin sulfate theoretically could help replace proteoglycan. Chondroitin sulfate has also been proposed to inhibit the action of some enzymes associated with cartilage breakdown and to have general anti-inflammatory properties. Data to support the proposed actions of chondroitin sulfate in in vitro studies have shown positive results. Definitive data to document the effect of chondroitin sulfate in living horses is not available at the present time. Data in other models (humans, rats, and dogs) does not automatically hold true for horses. So, the jury is still out with respect to chondroitin sulfate and its influence on joint health in horses.

Glucosamine is added to oral joint supplements either as hydrochloride or sulfate. As suspected, considerable debate exists as to the best form of glucosamine. Regardless of the exact chemical form, glucosamine is a significantly smaller molecule when compared to chondroitin sulfate. By most estimates, the absorption of glucosamine from the digestive tract does not seem to be a problem. However, specific horse absorption data have not been published in the scientific literature. If glucosamine is absorbed and if glucosamine reaches the joint, what is the potential mode of action? Glucosamine is a precursor to the disaccharide unit of glycosaminoglycan (GAG), which comprises the proteoglycan found in articular cartilage. In vitro data support the concept that glucosamine may stimulate synthesis of proteoglycan and collagen by chondrocytes. Experiments conducted in humans found glucosamine sulfate significantly more effective than placebo in improving pain and joint motion. Therefore, glucosamine may possess anti-inflammatory properties. Unfortunately, specific data in living horses are unavailable at the present time to definitively answer the questions surrounding the efficacy of glucosamine for joint health.

In addition to chondroitin sulfate and glucosamine, supplement manufacturers often include other ingredients necessary for synthesis of joint tissues. Included on the list of possible joint supplement additives are MSM (methylsulfonylmethane), copper, zinc, manganese, and vitamin C. MSM is a source of sulfur, a component that is necessary to strengthen collagen. The trace minerals copper, zinc, and manganese are each involved as cofactors for synthetic production of joint materials.

Finally, vitamin C is necessary for collagen formation. It is not known if these additives have any special benefit in oral joint supplements.

The bottom line regarding the efficacy of oral joint supplements is unclear. Many knowledgeable horsemen have used joint supplements on horses in their care with glowing success. Others have tried supplements and reported no detectable difference in their horses. Scientifically, many potentially promising benefits of oral supplements exist, but to date the efficacy of oral joint supplements in horses is unproven. Further, information on how much ingredient or which combination of ingredients is necessary to facilitate a joint response is totally absent. The unfortunate thing about the lack of definitive information is that many horse owners are considering themselves scientists and making their horses research subjects. The good news is that controlled research is being conducted to answer important questions surrounding oral joint supplements.

The Potential Problem with Joint Supplements

Do oral joint supplements actually contain the amount of active ingredient indicated on the label? This is a huge problem as published analytical reports conclude that 84% of human over-the-counter glucosamine/chondroitin products do not meet label claims. Another study on oral chondroprotective products intended for animals indicated that 70% of products did not meet label claim. With regulatory agencies overrun with new joint products, who is monitoring quality control of both raw ingredients and finished product? Further, who is policing labels and advertisements for implied drug claims? Are studies being done that will answer concerns regarding safety of joint products? These are all fair questions with few answers. Supplement manufacturers are beginning to appreciate the necessity of this information and have begun to organize themselves in an effort to answer consumer concerns.