

STRIDE®

Natural Mobility Supplement for Performance Horses

Stride - A Natural Mobility Feed Supplement.

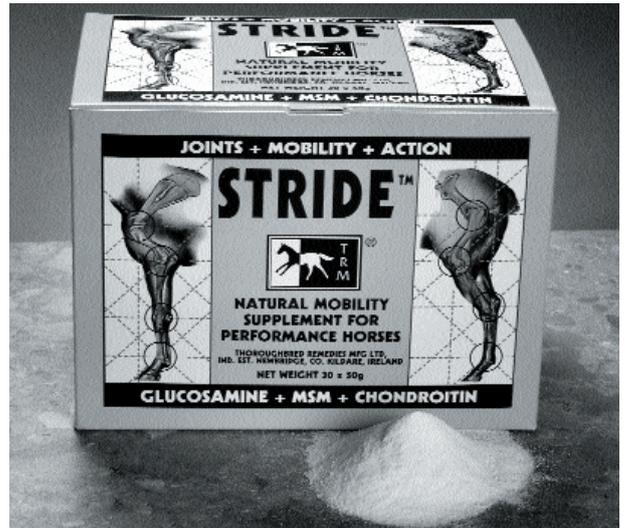
Stride is formulated as a feed supplement, to benefit the overall health of articular cartilage in the horse, and as a nutritional support in the healing process of connective tissue and cartilage.

Stride is a natural mobility supplement for performance horses. It contains only natural ingredients that are proven to alleviate joint problems. Degenerative Joint Disease (DJD) is a common malady of the horse. It most frequently strikes the hocks, the knees, front fetlocks and front navicular bones. DJD's consequences can be very severe. The health of articular cartilage depends on a delicate balance between the formation and the degradation of its components. Horse's joints are constantly asked to absorb shock and stress: the loading force of locomotion. The faster the gait, the greater the risk to the joint. Horse trainers are especially aware of the risks involved when asking their horses to perform at the highest level. There are several factors that can increase the risk of developing a degenerative joint problem. These include; trauma, age of the horse, the particular equine discipline and a genetic predisposition to disease. Cartilage, which is the 'last defence' for horse's joints, encounters shock on an ongoing basis. Previously, it was believed that cartilage tissue, once damaged, was irreparable. However, it is now acknowledged that the body is capable of creating the environment for cartilage tissue regeneration. Certain ingredients are required to replenish the components of the cartilage matrix.

These include :

- Glucosamine Hydrochloride
- Chondroitin sulphate
- Bio-available Sulphur (MSM Powder)

All three of these ingredients occur naturally in the body, and can therefore be classed as nutraceuticals. A nutraceutical is an orally administered substance, required for normal body structure and function, and administered with the intent of improving the health and well being of animals. These three ingredients work together as a natural mobility feed supplement. Cartilage is a very unusual tissue; because of the low cellular concentration in its matrix. Articular cartilage, which has such an important role to play in the protection of joints; and as a facilitator of non-frictional movement, is at a disadvantage when damaged, because it must repair itself with a self-limiting quantity of 'building blocks'. Not only does cartilage have this problem; but regeneration of the cartilage matrix, must also compete with the catabolic action of certain degradative enzymes released by the cartilage cells (chondrocytes). Glucosamine, MSM and



Chondroitin Sulphate are three ingredients that can support and speed up the healing process in the cartilage matrix. Some researchers have even indicated that these ingredients, not only have a natural tropism for cartilage, but may also have a prophylactic effect on the joint.^{1,2}

Active Ingredients Explained.

Glucosamine Hydrochloride.

Therapeutic Category: Antiarthritic.

Glucosamine is a 2-Amino-2-deoxyglucose compound. In other words, it is a simple protein (glutamine) and sugar molecule (glucose). Glucosamine is found in mucopolysaccharide (glycosaminoglycan) molecules such as hyaluronate, chondroitin sulphate and keratin sulphate. Glucosamine is essentially the building block for all the needed lubricants and shock absorbers in the body. These are technically known as glycosaminoglycans (GAG's) and proteoglycans (PG's). The natural conversion of glucose and glutamine to glucosamine in cartilage is not simple. There is a rate-limiting step in the entire sequence of events leading to the synthesis of cartilage tissue. Healthy cartilage in a given joint can only make a limited amount of glucosamine (damaged cartilage can make even less) no matter how much glucose and glutamine available. However, research has shown that the addition of glucosamine salts into the diet, could increase GAG production by 170%.³ Based on these results Karzel theorized that the addition of glucosamine by ingestion or injection would stimulate the production of GAG's and PG's in the cartilage by overcoming the joints inability to make enough glucosamine by itself. Further research undertaken in several European countries and in the Philippines compare very favourably with Karzel's early trials. All results were uniform in one thing: The addition of glucosamine in the diet could significantly improve osteoarthritic conditions in animal and human subjects because it stimulates cartilage regeneration. The oral dosage form of glucosamine is very suitable for treatment of joint problems as it is absorbed well, tolerated well and is simple to administer. There are three forms of Glucosamine commercially available ; N-Acetyl-Glucosamine,



Glucosamine Sulphate and Glucosamine Hydrochloride. N-acetyl-Glucosamine is metabolised selectively by the liver to make proteins, and is therefore less available to repair cartilage. Glucosamine hydrochloride is 83% glucosamine, it is more stable than glucosamine sulphate, it has a much higher concentration of glucosamine available than in the salt form, and it is sodium free.⁵

Chondroitin Sulphate.

Chondroitin sulphate is a high viscosity mucopolysaccharide (GAG). Chondroitin sulphate is the most abundant glycosaminoglycan (GAG) in the cartilage matrix. Chondroitin sulphate is also found in skeletal tissue and in the vascular system. Essentially, chondroitin sulphate has two roles to play with regard to cartilage. Chondroitin sulphates form a structural component of proteoglycans (PG's). PG's are the shock absorbers of cartilage by virtue of the high concentration of negative charges, which are capable of binding large amounts of water. This hydrostatic pressure is fundamental within the cartilage matrix, as it is this that gives the articular cartilage joint, the ability to be compressed, and then to revert back to its original anatomy. Secondly, chondroitin sulphate plays a very important role in the inhibition of degradative enzymes. Degenerative Joint Disease normally occurs when there is an altered cartilage metabolism. In other words, the rate of breakdown of cartilage is greater than the synthesis of new cartilage tissue.

Dr.Theodosakis, M.D., who wrote the very popular book "The Arthritis Cure." talked about the relationship between glucosamine and chondroitin sulphate: "*Working together synergistically, glucosamine and chondroitin sulphates stimulate the synthesis of new cartilage while simultaneously keeping the cartilage-bursting enzymes under control. This helps to normalise the cartilage matrix, in essence treating the disease at the cellular level. By itself, each supplement is effective. Together they may well be the answer for millions of people suffering from osteoarthritis*".

Methylsulfonylmethane (MSM)

Therapeutic Category: Proposed as analgesic and anti-inflammatory agent. MSM is organic sulphur, which is easily absorbed and usable by the body. It is found in almost every cell of every animal and plant. MSM is known to alleviate pain associated with systemic inflammatory disorders, most notably arthritis. The inclusion of MSM in Stride has three roles to carry out: **1.** MSM is a source of bio-available sulphur. This is a critical role, as sulphur is needed for the synthesis of connective tissue, hormones, many amino acids, hooves, hair and immunoglobulins. Scientific research strongly suggests that a horse requires a constantly maintained minimum concentration of 1 gram of bio-available sulphur per day. This is a maintenance level for the horse in perfect health. If the horse develops a joint problem, the amount of sulphur available must be increased in order to repair tissue. R. J. Herschler when writing in the *Equine Veterinary Data*, has this to say about MSM "A review of available literature sources indicates that sulphur has been overlooked where

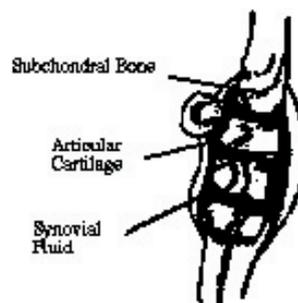
dietary deficiency is considered. No higher life form, plant or animal, can exist without bio-available sulphur".⁶ **2.** MSM exhibits an anti-inflammatory action, which is important in order to help ease pain and to increase mobility in the joint. **3.** Finally, MSM can help to sustain cell flow-through, allowing harmful substances to flow out, while at the same time permitting nutrients to flow in. This will speed up the time for inflammation to dissipate in a compromised joint. If the permeability of synovial fluid is changed in any way, it will affect the feeding status of chondrocytes (cartilage cells). Cartilage is an avascular tissue, therefore if the efficacy of the pathway of exchange, is altered in any way, (which is the case in an inflamed joint), there will be a shortage of the 'building blocks' needed for the rejuvenation of cartilage. Therefore MSM can be seen as a co-factor of Glucosamine and Chondroitin Sulphate in the repair of the cartilage matrix.

The Synovial Joint & Articular Cartilage.

The Synovial joint consists of the articulating surfaces of bone covered by the articular cartilage, a joint capsule, a cavity within these structures containing synovial fluid and associated ligaments. Stability of the joint is provided by the bony configuration of the joint and the ligamentous and capsular support systems. In addition there is a negative hydrostatic pressure within the synovial cavity of normal joints, and this is considered to impart 'suction' and stabilisation.

The three principle functions of synovial membrane are:

- Phagocytosis (breakdown & ingestion of unwanted substances)
- Regulation of protein and hyaluronate content of synovial fluid.
- Regeneration



The Synovial Joint.

Synovial fluid provides a pathway for exchange of nutrients and waste products between the general circulation and the articular chondrocytes, and provides lubrication. The hyaluronate fraction of joint fluid is responsible for this lubrication. Alterations of synovial membrane after a joint injury are reflected in changes of the synovial fluid composition. Changes in synovial fluid composition are particularly sensitive indicators of the degree of inflammation caused by a joint injury. Acute inflammation causes an increase in vascular permeability and altered metabolic activity within the synovial membrane. Changes in the concentration of synovial fluid may cause a reduction in the molecular weight of the hyaluronate being produced and a release of degradative enzymes. Hyaluronate is needed to form the backbone of proteoglycans, therefore a reduction in the content of this GAG may impair proper proteoglycan assembly.

Articular cartilage and function.

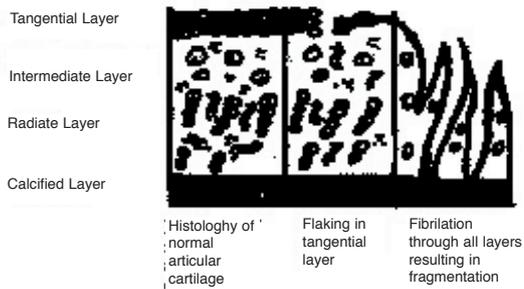
Normal articular cartilage appears milky and opaque in the



thicker regions but translucent with a slight bluish tinge in the thinner regions. Articular cartilage, when viewed histologically, has four layers of cells. The tangential layer is the top surface that articulates with synovial fluid. This layer is characterised by ovoid (flat) cells. The next layer is the intermediate layer. This layer contains larger chondrocytes (cells) and collagen fibrils. The radiate layer is next. This deep layer is characterised by chondrocytes arranged in vertical columns. The final layer, called the calcified layer is the mineralised part of cartilage. It is composed of mineralised cartilage and chondrocytes in the various stages of degradation. What can happen if there is joint dysfunction? A series of changes can occur in each layer of cartilage.

'Flaking' occurs when only the tangential layer is involved in the early stages of degenerative joint disease. As the

Histological Progression of DJD



erosion of cartilage continues deeper, it is referred to as 'fibrillation' since the surface appears as rows of filaments due to the degeneration along the vertical cellular columns. When the fibrillation is localised, blisters are formed by local oedema from a deterioration as deep as the intermediate layer. This malign cycle of erosion will leave areas devoid of cartilage, which encourages the formation of new bony tissue from the subchondral bone. Therefore the joint will lose its compressibility. The stage and the progression of disease will affect the efficacy of the chosen treatment. If, however there is an early diagnosis, Stride will help produce the new components needed to restore a healthy cartilage matrix.

There are four major structural components of cartilage.

- Collagen
- Proteoglycans
- H₂O
- Cell (chondrocytes)

Collagen

Collagen is the most abundant protein in the body. The concentration of collagen is highest in the tangential layer of the articular cartilage and falls sharply with increasing distance from the surface. The proteoglycan content shows a trend in the other direction. The collagen making process depends on a steady flow of nutrients, including sugars, protein, vitamin C, Fe, Cu and Mn. If any of these are in short supply, the manufacture of collagen is impaired. The addition of specialised sugars on the collagen fibre determines its strength. Certain nutrients (Glucosamine) can convert themselves into these essential sugars, and this enhances the repair of joints. Collagen health is critical to cartilage, as it is this component that gives cartilage its tensile strength and holds the proteoglycan structures in check. Glucosamine is involved in the synthesis of collagen because it stimulates

procollagen

production, which is a precursor to collagen. **MSM** powder provides a bio-available source of sulphur for the production of collagen and some amino acids (methionine) that are also needed for collagen synthesis.

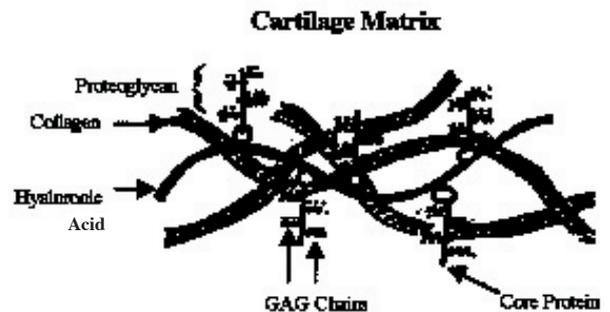
Proteoglycans.

Proteoglycans are a combination of protein and sugar. They have a basic structure of a core protein to which numerous glycosaminoglycan (GAG) side chains are attached. Proteoglycans fill up the extracellular spaces in cartilage not taken up by collagen. Their function is to soak up water within the tissue to swell like a sponge. There is not enough space for the proteoglycans to soak up all of the water within the tissue. This creates a hydrostatic pressure or 'swelling tension' held in check by collagen. This hydrostatic pressure is what gives cartilage its ability to absorb shock and resist compression. Cartilage is unique among other tissues because of its high content of glycosaminoglycans.

These include: Chondroitin sulphate
Keratin Sulphate
Hyaluronate

These GAG's have the ability to attract water molecules, and this is what makes cartilage an effective cushion for the joint. **Glucosamine** is a precursor to all of these glycosaminoglycans. TRM's Stride also includes an extra source of one GAG, Chondroitin sulphate. This is because: **a)** Chondroitin sulphate is the most abundant GAG in articular cartilage and **b)** Chondroitin sulphate has an inhibiting effect on certain enzymes that breakdown cartilage tissue. **MSM** provides a bio-available source of sulphur for the production of chondroitin sulphate, keratin sulphate and collagen.

Diagram of Cartilage Matrix & Proteoglycan aggregate.



Cartilage Cells-Chondrocytes.

The only cells present in cartilage are chondrocytes. Their role is to produce and maintain cartilage. Cartilage tissue is avascular (no blood or lymph is channelled into the tissue), therefore it is deficient in the oxygen and nutrients needed for growth. Like bone, cartilage is constantly remodelling and repairing itself. Chondrocytes must receive nutrition from synovial fluid. Once again we can see the importance of maintaining the integrity of synovial fluid. If the hyaluronate content is reduced, cartilage cells may be starved of the nutrients needed for cartilage regeneration. This situation is worsened if there is a lot of activity from the enzymes responsible for cartilage breakdown. The inclusion of Glucosamine and Chondroitin sulphate in Stride, will help to reverse this situation by stimulating hyaluronate production and slowing down metabolic breakdown of cartilage components.



Stride – The Scientific Evidence.

In 1969, the first clinical trials took place to investigate the effectiveness of glucosamine as a therapeutic agent for osteoarthritis. German physicians, using an injectable preparation of 400mg of glucosamine sulphate reported a substantial reduction of pain often accompanied by increased mobility.⁷ A number of controlled evaluations of oral glucosamine sulphate appeared in the early 1980's. Double-blind trials were conducted in Italy, France, Portugal and the Philippines.^{8,9,10,11} The results of these studies were uniform. Glucosamine therapy was associated with a gradual and progressive reduction of articular pain and tenderness, and an improvement in the range of motion of the affected joint. Increased walking speeds were also reported in some studies. Of significant importance, was the fact that, all of the double blind trials reported a complete absence of side effects with oral glucosamine. This is a very significant finding as traditional treatment with NSAID's can induce unwelcome side effects, such as stomach cramp and ulcerative conditions. The treatment with oral glucosamine was preferred in all of these studies because it is easy to administer and well tolerated. Unlike NSAID's or intra-articular injections it is not an expensive method of treatment, neither is it time consuming for either the veterinarian or the owner of the horse. Probably the most significant fact of all these studies, is that unlike NSAID's, glucosamine salts may actually reverse the conditions of degenerative joint disease, thereby treating the disease at the cellular level. NSAID's, while they provide palliative analgesia, do nothing to redress the fundamental problem, and indeed have been shown to slow the rate of proteoglycan synthesis, potentially exacerbating the loss of cartilage.¹² Research undertaken by Setnikar in 1991 indicated that oral glucosamine is well absorbed and unlike NSAID'S does not irritate the gastrointestinal tract.¹³ Several studies also reported that therapeutic benefits were substantially conserved for over a month after therapy was discontinued, whereas any supposed benefit of placebo therapy was rapidly lost. In another study, the initial response from a well-known NSAID (Ibuprofen) was rapid pain relief as compared to glucosamine. However improvement with glucosamine was gradual but progressive. By week 8 the benefits and analgesia from glucosamine was significantly better than that from ibuprofen after 8 weeks.¹⁴ Chondroitin sulphate has also been studied for its antiarthritic effect. The most common finding in these studies was the chondroprotective activity that oral chondroitin sulphate has on articular joints. In one study carried out in Italy in 1995, researchers found that after only five days of oral chondroitin sulphate administration, they discovered a significant increase in concentration and molecular mass of hyaluronate and a decrease of the degradative enzyme, N-acetyl-glucosaminidase.¹⁵ Like glucosamine, chondroitin sulphate is well absorbed into the gastrointestinal tract, has little or no side effects and did not have any symptoms of local or general toxicity.¹⁶ A prominent factor of this literary review of scientific research, was the positive and benign effects, both glucosamine and chondroitin sulphate had in the treatment of osteoarthritis. It is very rare to hear about a possible cure for degenerative joints, never mind an effective treatment that is simple, well tolerated, inexpensive and exhibits chondroprotective properties.

Stride is a special formulation that includes Glucosamine, Chondroitin Sulphate and MSM: all of which help speed up and support the healing process in damaged joints.

Glossary of Terms.

Analgesic-A compound capable of producing analgesia i.e., one that relieves pain as there is a reduced response to painful stimuli.

Anti-inflammatory-Reducing inflammation by acting on body mechanisms, without directly antagonising the causative agent.

Chondrocyte-The cartilage cells.

Collagen-The major protein (comprising over half of that in mammals) of the white fibres of connective tissue, cartilage and bone.

Catabolism-The breaking down, in the body of complex chemical compounds into simpler ones, often accompanied by the liberation of energy. 2. The sum of all degradative processes.

Glycosaminoglycan (GAG's)-Protein-polysaccharide complex obtained from proteoglycans and containing as much as 95% polysaccharide (sugars).

NSAID-Non steroidal anti-inflammatory drug. Indicated for musculoskeletal conditions, where relief from pain and a reduction in the associated inflammation is required.

Nutraceutical-A substance which is produced in a purified or extracted form and administered orally to patients, to provide agents required for normal body structure and function, and administered with the intent of improving the health and well-being of animals. (N.A.V.N.C.)

Palliative-Reducing the severity, without curing the underlying cause. (Alleviation of the symptoms).

Prophylactic-Preventing disease, an agent that acts to prevent a disease.

Proteoglycan-Glycosaminoglycans bound to protein chains in covalent complexes. They occur in the extracellular matrix of the cartilage tissue. Important characteristic of proteoglycans is their ability to soak up fluid.

Phagocytosis-The process of ingestion and digestion by cells of solid substances e.g. synovial cells that ingest dead tissue and degenerated chondrocytes.

Synthesis-A building up, putting together or formation of compounds.

¹ Setnikar, R. Palumbo, S. Canali, and G.Zanola. Pharmacokinetics of Glucosamine in Man., *Arzneim. Forsch/Drug Res.* 43 (II), Nr.10 (1993).

² Drovanti, A., et al., Therapeutic activity of oral glucosamine sulphate in osteoarthritis: A placebo controlled double-blind investigation. *Clinical Therapeutics* Vol. 3No.4, (1980).

³ Karzel, K. Domenjoz, R. Effects of Hexamine Derivatives and Uronic Acid Derivatives on glycosaminoglycan Metabolism of Fibroblast Cultures, *Pharmacology* 5:337-345 (1971).

⁴ Drovanti, A et al., Therapeutic Activity of Oral Glucosamine Sulphate in Osteoarthritis: A Placebo-Controlled Double-Blind Study. *Clinical Therapeutics* Vol. 3 No. 4. 1980:260-272.

⁵ Bucci, Luke, PhD, "Pain Free" The Summit Group.

⁶ Herchler R.J., MSM:A Nutrient for the Horse. *Equine Veterinary Data.*, Vol. 7, No.17. pp268-269.

⁷ Bohne W., Glukosamine in der konservativen Arthrosebehandlung. *MEd Welt* 1969;30 pp1668.

⁸ Crolle G., Glucosamine sulphate for the management of arthrosis: a controlled clinical investigation. *Curr Med Res Opin* 1980;7: 104-109.

⁹ Drovanti A et al., Therapeutic activity of oral glucosamine sulphate in osteoarthritis : A placebo controlled double-blind investigation. *Clin Ther* 1980: 3260-272.

¹⁰ D'Ambrosio E, Casa B, Bompani R et al., Glucosamine sulphate: a controlled clinical investigation in arthrosis, *Pharmatherapeutica* 1981; 2:504-508.

¹¹ Pujalte, J., et al., Double-blind Clinical Evaluation of Oral Glucosamine Sulphate in the Basic Treatment of Osteoarthritis. *Curr Med Res Opin* 7(2) 110-114 (1980).

¹² McCarthy, M. F., *Medical Hypothesis*, 1994 42. 323-327.

¹³ Setnikar I et Al., Antiarthritic effects of glucosamine sulphate studied in animal models. *Arzeim-Forsch* 1991; 41 542-545.

¹⁴ Vas A L. Double-blind clinical evaluation of the relative efficacy of ibuprofen and glucosamine sulphate in the management of osteoarthritis of the knee in out-patients. *Curr Res Opin* 1982; 8.

¹⁵ Conte A., et al., Biochemical and Pharmacokinetic Aspects of Oral Treatment with Chondroitin Sulphate. *Arzneim-Forsch/Drug Res* 45 (11), N0.8 (1995.)

¹⁶ Conte A., et al., Biochemical and Pharmacokinetic Aspects of Oral Treatment with Chondroitin Sulphate. *Arzneim-Forsch/Drug Res* 45 (11), N0.8 (1995).

Analysis, Presentation and Packaging.

Composition	per 50g	per1Kg
Glucosamine Hydrochloride	3600mg	72000mg
Chondroitin Sulphate	2375mg	47500mg
MSM (Methylsulfonylmethane)	10000mg	200000mg
Excipient to	50g	1000g

Stride is presented in a 50g sachet for ease of administration as a daily dose. Stride sachets are packed as a unit of 30 sachets in an attractive presentation box.

