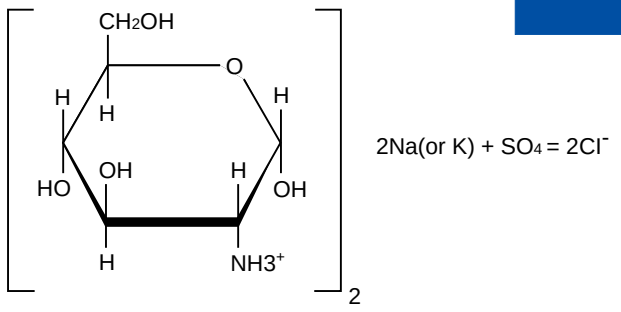
Monograph



Glucosamine Sulfate

Summary

Glucosamine sulfate's role in halting or reversing joint degeneration appears to be directly due to its ability to act as an essential substrate for, and to stimulate the biosynthesis of, the glycosaminoglycans and the hyaluronic acid backbone needed for the formation of the proteoglycans found in the structural matrix of joints. Successful treatment of osteoarthritis must effectively control pain and should slow down or reverse the progression of the degeneration. Biochemical and pharmacological data combined with animal and human studies demonstrate that glucosamine sulfate is capable of satisfying both of these criteria.

Introduction

Glucosamine is the most fundamental building block required for biosynthesis of the classes of compounds including glycolipids, glycoproteins, glycosaminoglycans (formerly called mucopolysaccharides), hyaluronate, and proteoglycans. As a component of these macromolecules, glucosamine has a role in the synthesis of cell membrane lining, collagen, osteoid, and bone matrix. Glucosamine is also required for the formation of lubricants and protective agents such as mucin and mucous secretions.

Pharmacokinetics

In humans, about 90 percent of glucosamine, administered as an oral dose of glucosamine sulfate, is absorbed from the digestive tract.[1] After an oral dose, glucosamine concentrates in the liver, where it is either incorporated into plasma proteins, degraded into smaller molecules, or utilized for other biosynthetic processes.[1] Elimination of glucosamine is primarily through the urine, with a small amount of glucosamine or its derivatives eliminated in the feces.[2, 3]

Mechanism of Action

Glucosamine sulfate is capable of stimulating proteoglycan synthesis, inhibiting the degradation of proteoglycans, and stimulating the regeneration of experimentally-induced cartilage damage.[4,5] Some experts also believe glucosamine sulfate might promote the incorporation of sulfur into cartilage.[6]

Clinical Research on Osteoarthritis

The primary therapeutic use of glucosamine sulfate has been in the treatment of degenerative diseases of the joints. Although many of the available studies have compared glucosamine sulfate to placebo, in the trials where glucosamine sulfate has been compared to NSAIDs, long-term reductions in pain are greater in patients receiving glucosamine sulfate.[7-11]

Symptoms such as articular pain, joint tenderness, and swelling often improve following a 6-8 week period of oral administration of glucosamine sulfate.[7-13] For most individuals, an expectation of a

reduction in symptoms of from 50-70 percent is reasonable.[7] Improvements secondary to glucosamine sulfate therapy generally are sustained six to 12 weeks following cessation of the treatment regimen.[12]

For arthritis of the knee, evidence suggests that about 60 percent of patients will have a good to excellent response to this intervention, while an additional 35 percent will have a more moderate benefit. Preliminary evidence suggests patients with arthritis of the shoulder or elbow respond the best to glucosamine sulfate (about 75 percent judged as good and only one percent judged as insufficient), while polyarticular arthritis and arthritis of the hip had the poorest response rate (only 43 percent and 49 percent, respectively).[12]

Toxicity

No LD50 is established for glucosamine sulfate, since even at very high levels (5000 mg/kg oral, 3000 mg/kg i.m., and 1500 mg/kg i.v.) there is no mortality in mice or rats.[14]

The incidence of mild side-effects secondary to oral administration of glucosamine sulfate is reported to be 6-12 percent. The most commonly reported side-effects include gastrointestinal disturbances (such as epigastric pain/tenderness, heartburn, diarrhea, nausea, dyspepsia, vomiting, and constipation), drowsiness, headaches, and skin reactions. These complaints are generally mild in character and are reversed when treatment with glucosamine sulfate is discontinued.[11,12]

Glucosamine sulfate has been administered safely to patients with a variety of disease conditions, including circulatory disease, liver disorders, diabetes, lung disorders, and depression, with no observed interference with either the course of the illness or pharmacological treatment for the conditions.[8] However, some concern exists regarding the use of glucosamine sulfate by individuals with type II diabetes, since evidence is suggestive of glucosamine sulfate contributing to insulin resistance, possibly contributing to glucose toxicity in insulin-sensitive tissues.[15] Evidence also indicates that individuals with active peptic ulcers and individuals taking diuretics tend to have an increased incidence of side effects from glucosamine sulfate.[12]

Dosage

The advised oral dosage routine for glucosamine sulfate is 500 mg three times daily for a minimum of six weeks. Since obesity has been associated with a below average response to glucosamine sulfate,[12] a higher dose might be required by these individuals.

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