Glucosamine

Technical Background

• Glucosamine is a simple amino-sugar. It is synthesized from glucose (a sugar) and glutamine (an amino acid).¹
• Glucosamine is wide spread in nature. It is a basic building block of chitin, the polymeric molecule that forms the cell walls of fungi and the external skeletons or shells of insects, shrimp, and crabs.¹
• Glucosamine is also a basic building block of animal and human cartilage, the tissue that lines, cushions and lubricates skeletal joints. Cartilage is a complex matrix of collagen fibers interwoven with proteoglycan molecules. The proteoglycans are large and complex macromolecules comprised of long chains of polymerized amino-sugars (a principle one being glucosamine). Proteoglycans provide a framework for the collagen matrix. They also hold water to give the cartilage flexibility, resiliency, and resistance to compression.²,³
• The synthesis of glucosamine from glucose and glutamine is thought to be a rate-limiting step in the ultimate production of proteoglycans. Therefore, higher levels of glucosamine in the chondrocytes (cells that manufacture the building blocks of cartilage) promote the production of higher levels of proteoglycans.⁴
• In addition, glucosamine is though to play a regulatory role in proteoglycan formation by stimulating proteoglycan biosynthesis and inhibiting proteoglycan degradation.⁴
• Because of its important role in regulating cartilage formation, glucosamine has been used clinically in the treatment of osteoarthritis. Several double-blind, placebo controlled clinical trials, run principally in Europe, have shown oral administration of glucosamine sulfate, at dosages of 1200-1500 mg per day to be an effective treatment for this disorder.⁵,⁶,⁷,⁸,⁹,¹⁰,¹¹,¹² Benefits include reduced joint pain and stiffness, improved joint mobility, and reversal of cartilage loss. Few if any negative side effects have been reported.
• A variety of glucosamine supplements are available on the market today. The better formulations contain one or more of the nutrient cofactors required for cartilage formation, namely vitamin C, manganese, and silicon.
• Many glucosamine supplements also contain chondroitin sulfate. Chondroitin is one of the long chain polymers that make up proteoglycans. With a molecular weight on the order of 50,000, there is great doubt as to whether oral chondroitin passes through the wall of the gut, to become available for cartilage synthesis. Furthermore, there is
no firm clinical evidence to date suggesting that chondroitin sulfate adds anything but cost to glucosamine supplements. Preliminary studies suggests that glucosamine alone is every bit as effective as the combination product.

**Sources and Recommended Intake**
- Glucosamine is not considered to be an essential nutrient, therefore it has no established RDA.
- Foods that contain polymerized glucosamine in the form of chitin or cartilage include mushrooms, whole shellfish, whole chicken, beef, and fish. It is debatable whether significant amounts of simple glucosamine are made available during cooking of these foods. Some animal gelatin preparations may contain significant amounts of free glucosamine.
- Clinical research on the benefits of oral glucosamine supplements for osteoarthritis have typically shown that 1,500 mg per day is an effective dose.5-11

**Abstracts**

**Reginster JY, Deroisy R, Rovati LC, Lee RL, Lejeune E, Bruyere O, Giacovelli G, Henrotin Y, Dacre JE, Gossett C. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial.** Lancet. 2001 Jan 27;357(9252):247-8. BACKGROUND: Treatment of osteoarthritis is usually limited to short-term symptom control. We assessed the effects of the specific drug glucosamine sulphate on the long-term progression of osteoarthritis joint structure changes and symptoms. METHODS: We did a randomised, double-blind placebo controlled trial, in which 212 patients with knee osteoarthritis were randomly assigned 1500 mg sulphate oral glucosamine or placebo once daily for 3 years. Weightbearing, anteroposterior radiographs of each knee in full extension were taken at enrolment and after 1 and 3 years. Mean joint-space width of the medial compartment of the tibiofemoral joint was assessed by digital image analysis, whereas minimum joint-space width--ie, at the narrowest point--was measured by visual inspection with a magnifying lens. Symptoms were scored by the Western Ontario and McMaster Universities (WOMAC) osteoarthritis index. FINDINGS: The 106 patients on placebo had a progressive joint-space narrowing, with a mean joint-space loss after 3 years of -0.31 mm (95% CI -0.48 to -0.13). There was no significant joint-space loss in the 106 patients on glucosamine sulphate: -0.06 mm (-0.22 to 0.09). Similar results were reported with minimum joint-space narrowing. As assessed by WOMAC scores, symptoms worsened slightly in patients on placebo compared with the improvement observed after treatment with glucosamine sulphate. There were no differences in safety or reasons for early withdrawal between the treatment and placebo groups. INTERPRETATION: The long-term combined structure-modifying and symptom-modifying effects of glucosamine sulphate suggest that it could be a disease modifying agent in osteoarthritis.

**McCarty MF. The neglect of glucosamine as a treatment for osteoarthritis – a personal perspective. Medical Hypotheses 1994; 42: 323-327.** Osteoarthritis results from progressive catabolic loss of cartilage proteoglycans, owing to an imbalance between synthesis and degradation. Standard drug therapy is only of palliative benefit and may exacerbate loss of cartilage. Glucosamine is an intermediate in mucopolysaccharide synthesis, and its availability in cartilage tissue culture can be rate-limiting for proteoglycan production. A number of double-blind studies dating from the early 1980’s demonstrate that oral glucosamine decreases pain and improves mobility in osteoarthritis, without side effects. Nevertheless, medical researchers and
physicians in the US have totally ignored this ration and safe therapeutic strategy. By mechanisms that are still unclear, the natural methyl donor S-adenosylmethionine also promotes production of cartilage proteoglycans, and is therapeutically beneficial in osteoarthritis in well-tolerated oral doses. These and other safe nutritional measures supporting proteoglycan synthesis may offer a practical means of preventing or postponing the onset of osteoarthritis in older people or athletes.

References