

Glucosamine

History

- Glucosamine has been used clinically in Europe since the 1960s.
- Became very popular in the United States in the mid-1990's with the publication of popular best-sellers such as "The Arthritis Cure" by Jason Theodosakis.
- Now the most popular dietary supplement in the United States with annual sales of more than \$200 million per year.
- Most commercial glucosamine is prepared from the shells of crabs and other shell fish.

Most studied use

Osteoarthritis

Summary of the evidence

- There is reasonably good evidence that glucosamine reduces the symptoms of osteoarthritis and possibly slows the long-term progression of the disease as well.
- Glucosamine is well tolerated with minimal adverse effects or drug interactions.
- Although often used in combination with chondroitin, there no data to asses whether their effects are additive or how they compare.

Pharmacology

- In humans, glucosamine is a key building block for glycosaminoglycans and hyaluronic acid, thereby serving as a substrate for the production of articular cartilage.
- Glucosamine is a small, easily absorbed amino sugar. Though easily absorbed, its bioavailability is still less than 20% due to a high first pass effect in the liver.

Mechanism of action

- Mechanism of analgesic effect is unknown, but the onset of action is longer than for NSAID's. Glucosamine does not appear to affect the cyclooxygenase system.
- In animal studies, glucosamine is incorporated rapidly into cartilage, and when added to fibroblast cultures, glucosamine increases the production of glycosaminoglycans.
- By increasing supply of substrate, may help to build up the absorbent extra-cellular matrix of cartilage, and over time may slow the degradation of articular surfaces.

Clinical studies

- A Cochrane review of glucosamine therapy for osteoarthritis found 16 RCT's which met inclusion criteria (1980-1999). 13 RCT's compared glucosamine to placebo and in all except one glucosamine was found to be superior. (Towheed 1999)
- A more recent, even more rigorous meta-analysis (McAlindon 2000) found 6 RCT's which met more stringent inclusion criteria. Pooling the results from the 911 patients in these trials yielded an overall effect size highly in favor of glucosamine ($p=.05$).
- Since these two meta-analyses, a high quality study tested glucosamine vs. placebo in 212 patients followed for an average of 3 years (Reginster 2001). This study found a highly significant benefit from glucosamine in terms of symptom and function scores, as well as prevention of joint space narrowing on knee x-rays.

Adverse effects

- Gastrointestinal effects including epigastric pain, diarrhea and constipation have been reported but these are generally similar to placebo.

Contraindications/cautions

- Caution is suggested in diabetic patients. Glucosamine has been shown in-vitro and in animal experiments to increase insulin resistance by entering the hexosamine biosynthetic pathway. The clinical significance of this is not known. Diabetics should be carefully monitored to detect any changes in glucose control.
- Theoretically, patients who have seafood allergies should avoid glucosamine which is derived from shellfish, although no case reports of such reactions have been published. Unfortunately, labels on glucosamine products do not usually identify their source.

Important drug/herb interactions

- No important interactions. Use in combination with NSAID's appears to be safe.

Formulation and dosage

- The dose tested in most clinical trials has been 500 mg tid, although the largest trial by Reginster tested 1500 mg qd.
- All trials have tested glucosamine *sulfate* rather than glucosamine *hydrochloride*.
- Patients should be warned that symptom relief may take up to 8 weeks to become apparent, which is longer than patients may be used to with NSAID's.

Key Glucosamine References

1. McAlindon TE, et al. Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. *JAMA* 2000;283:1469-1475.
2. Towheed TE, et al. Glucosamine therapy for treating osteoarthritis (Cochrane Review). In: *The Cochrane Library*, Issue 2, 2003. Oxford: Update Software.
3. Reginster JY, et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. *Lancet*. 2001;357:251-6.

For Additional Information

1. Natural Medicines Comprehensive Database. Available through UW Healthlinks.
2. About Herbs. <http://www.fammed.washington.edu/predoctoral/CAM/sites.html>.
3. Herbmed.org for more general background.
4. For information about the quality of specific brands, check Consumerlabs.com.

