

Glucosamine Efficacy Information

The efficacy of glucosamine has been evaluated through animal models and human clinical trials over many decades. Glucosamine is commonly used "as a single ingredient or in combination with other ingredients" as "a joint builder (to increase joint flexibility, to restore joint function, and to alleviate joint pain), and for osteoarthritis" (IOM 2003). Glucosamine is "a major building block of the water-loving proteoglycans" which are used to produce glycosaminoglycans, which bind water in the cartilage matrix (Theodosakis 2004). Glucosamine HCl has been radiolabeled and administered to both rats and dogs (Setnikar 1984, 1986), showing it is readily absorbed.

In two recent meta-analyses (McAlindon 2000, Richy 2003), researchers reviewed the evidence for efficacy of glucosamine HCl and glucosamine sulfate for arthritic complaints. It was concluded that glucosamine was moderately efficacious for relief of arthritic complaints, and that glucosamine had highly significant efficacy on all aspects of knee osteoarthritis including joint space narrowing, pain, and mobility scores. In 2 recent major clinical trials (Clegg 2006, Herrero-Beaumont 2005) glucosamine was supplied at 1,500 mg/day to osteoarthritis patients, and positive results indicate that glucosamine reduced knee pain compared to a placebo, and that all treatments were well-tolerated by the study subjects.

Glucosamine is commonly found in several salt forms, including glucosamine hydrochloride (HCl), glucosamine sulfate and N-acetylglucosamine (IOM, 2003). "The counter anion of the glucosamine salt (i.e. chloride or sulfate) is unlikely to play any role in the action or pharmacokinetics of glucosamine" (PDR, 2001), as orally administered glucosamine HCl and glucosamine sulfate are both dissociated in the stomach and free glucosamine then enters the small intestine (Anderson 2005). Glucosamine HCl does contain 83% free base glucosamine compared to only 65% in glucosamine sulfate (PDR, 2001). It has been concluded through *in vitro* testing that glucosamine HCl and glucosamine sulfate have similar abilities to prevent or reduce cartilage degeneration (Karzel 1971, Karzel 1982, Fenton 2000). A direct comparison of glucosamine HCl to glucosamine sulfate (Karzel 1971, Karzel 1982) showed equality in stimulation of proteoglycan synthesis. A recent human clinical study directly compared glucosamine HCl and glucosamine sulfate on a glucosamine basis (versus a weight basis) and reported no difference in response among groups (Qiu 2005).

Key Findings

- Chronic joint problems and arthritis affect close to 1/3 of American adults. *CDC, 2002*
- Orally administered glucosamine is rapidly absorbed. *Setnikar, 1993*
- Glucosamine is an important building block of the joint tissue that forms a cushioning layer at the end of bones. *IOM, 2003*
- Glucosamine has a much lower incidence of side effects than NSAIDs, or even placebo. *Anderson, 2005*
- 1,500 mg of glucosamine is a typical daily dose. This level of supplementation has shown pain relief for people coping with regular knee pain. *Reginster, 2001, Clegg 2006, Herrero-Beaumont 2005*
- A 3-year study showed a 20-25% symptomatic improvement in the glucosamine group, while they worsened in the placebo group. *Pavelka, 2002*
- Joints in patients who took glucosamine narrowed by a mean of only 0.06 mm, compared to 0.31 mm in the placebo group. *Reginster, 2001*

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GLUCOSAMINE HYDROCHLORIDE REFERENCES

2006: Clegg DO, Reda DJ, Harris CL et al. Glucosamine, chondroitin sulfate and the two in combination for painful knee osteoarthritis. *N Engl J Med* 2006; 354:795-808.

2005: Anderson JW et al. Glucosamine effects in humans: a review of effects on glucose metabolism, side effects, safety considerations and efficacy. *Food Chem Toxicol.* 2005 Feb;43(2):187-201.

2005: Qiu GX, et al. A multi-central, randomized, controlled clinical trial of glucosamine hydrochloride/sulfate in the treatment of knee osteoarthritis. *Natl. Med. J. China.* 2005 Nov 16;85(43):3067-70.

2004: Theodosakis, Jason MD. The Arthritis Cure, The Revised Edition. St. Martins Press, 2004.

2003: Braham R, et al. The effect of glucosamine supplementation on people experiencing regular knee pain. *Br J Sports Med.* 2003; 37:45-49.

2003: Institute of Medicine. Safety review: Draft 3 prototype monograph on glucosamine. pp 1-84. 2003. Washington, DC, National Academy of Sciences. Ref Type: Report.

2003: Richey F, et al. Structural and symptomatic efficacy of glucosamine and chondroitin in knee osteoarthritis: a comprehensive meta-analysis. *Arch Intern Med.* 2003; 163:1514-1522.

2001: Hendler SS, et al. Glucosamine. *PDR for Nutritional Supplements*, First Edition. 2001. 186-189.

2000: Fenton JI, et al. *Osteoarthritis and Cartilage.* 2000;8, 444-451.

1999: Das A, et al. Combination of glucosamine and chondroitin in knee OA. *Osteoarthritis Cartilage.* 2000;8(5):343-350.

1999: Leffler CT, et al. "Glucosamine, chondroitin, and manganese ascorbate for degenerative joint disease of the knee or low back: a randomized, double blind, placebo-controlled pilot study." *Military Medicine* February 1999;164:2:85-91.

1986: Setnikar I, Giacchetti C, Zanolo G. Pharmacokinetics man. *Drug Res* 1986;36(1):729-735.

1984: Setnikar I, Giacchetti C, Zanolo G. Absorption, distribution and excretion of radioactivity after a single intravenous or oral administration of [¹⁴C] Glucosamine to the rat. *Pharmotherapeutica* 1984; 3 (38) 538-558.

1982: Karzel K, et al. "Effect of hexosamine derivatives on mesenchymal metabolic processes of in vitro cultured fetal bone explants" *Z. Rheumatology* 1982 Sep-Oct;41(5):212-8.

1971: Karzel K, et al. "Effect of hexosamine derivatives and uronic acid derivatives on glycosaminoglycan metabolism of fibroblast cultures." *Pharmacology* 1971;5:337-345.

GLUCOSAMINE REFERENCES

2005: G. Herrero-Beaumont et al. Effects of Glucosamine Sulfate on 6-Month Control of Knee Osteoarthritis Symptoms vs. Placebo and Acetaminophen: Results from the Glucosamine Unum in Die Efficacy (GUIDE) Trial. American College of Rheumatology, presentation #1203, Nov. 2005.

2003: Scroggie DA, et al. The effect of glucosamine-chondroitin supplementation on glycosylated hemoglobin levels in patients with type 2 diabetes mellitus. *Arch Intern Med* 2003; 163:1587-1590.

2002: Centers for Disease Control and Prevention, press release.

2002: Pavelka K, et al. Glucosamine sulfate use and delay of progression of knee osteoarthritis: a 3-year, randomized, placebo-controlled, double-blind trial. *Arch Intern Med* 2002; 162:2113-2123.

2001: Nguyen P, et al. "A randomized double-blind clinical trial of the effect of chondroitin sulfate and glucosamine hydrochloride on temporomandibular joint disorders: a pilot study." *Cranio* 2001;Apr;19(2):130-9.

2001: Reginster JY et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomized, placebo-controlled clinical trial. *Lancet* 2001; 357:251-256.

2000: Beren J, et al. "The therapeutic effect of glucosamine HCl/chondroitin sulfate combination of type II collagen-induced arthritis in D/A rats." Published in the Proceedings of the Society for Experimental Biology and Medicine, 2000.

2000: Hungerford et al. "Use of Nutraceuticals in the Management of Osteoarthritis." *Journal of the American Nutraceutical Association* 2000; Vol.3, No. 1:23-27.

2000: Lippiello L, et al. "Dose response and synergistic effect of glucosamine HCl and chondroitin sulfate on in-vitro proteoglycan synthesis by bovine and human chondrocytes." Paper presented at the 67th annual meeting of the American Academy of Orthopedic Surgeons, Orlando, FL, 2000.

2000: McAlindon TE, et al. Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. *J Amer Med Assoc* 2000; 283:1469-1475.

1999: Canapp SO, et al. "Scintigraphic evaluation of glucosamine HCl and chondroitin sulfate as treatment for acute synovitis in dogs." *American Journal of Veterinary Research* December, 1999;60(12):1550-1556.

1999: Lippiello L, et al. "Beneficial effect of cartilage disease-modifying agents tested in chondrocyte cultures and a rabbit instability model of osteoarthritis." *Arthritis & Rheumatology* September 1999;42(9)(supplement S256).

1998: Shankland WE. The effects of glucosamine and chondroitin sulfate on osteoarthritis of the TMJ: a preliminary report of 50 patients. *J Craniomandibular Practice* 1998; 16:230-235.

1993: Setnikar I, et al. Pharmacokinetics of Glucosamine in Man *Arzneimittel-Forschung.* 1993;43 (II), 10, 1109-1113.