

# Do glucosamine or chondroitin cause regeneration of cartilage in osteoarthritis?

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## \* EVIDENCE-BASED ANSWER

No direct evidence suggests glucosamine or chondroitin cause regeneration of cartilage in osteoarthritis. Use of glucosamine sulfate in knee osteoarthritis prevents joint space narrowing on radiographs (strength of recommendation [SOR]: B, based on 1 randomized controlled trial).

Intramuscular chondroitin polysulfate prevents radiographic progression of finger osteoarthritis (SOR: B, based on 1 randomized controlled trial).

Both chondroitin sulfate and glucosamine sulfate stimulate chondrocyte growth in vitro and in animal models (SOR: D, based on several bench research studies).

## \* EVIDENCE SUMMARY

A systematic review of glucosamine sulfate use for osteoarthritis, based on early research (1956-1991), found that it has anti-inflammatory properties and rebuilds damaged cartilage. (1) These studies evaluated chondrocytes grown in culture and animal models. (1,2) Chondroitin sulfate also stimulates chondrocyte biosynthesis in both animal and in vitro studies. There is insufficient evidence to demonstrate glucosamine sulfate or chondroitin sulfate stimulates chondrocyte growth in humans with osteoarthritis. (2,3)

Joint space narrowing on radiographs suggests progression of osteoarthritis. This narrowing is thought to imply cartilage destruction or loss due to osteoarthritis. A double-blinded randomized controlled trial studied the effect of glucosamine sulfate on tibial-femoral compartment joint space narrowing in 212 patients older than 50 with mild to moderate knee osteoarthritis. (4) Patients took either 1500 mg/day of glucosamine sulfate or placebo over 3 years. Knee radiographs in a standing anterior-posterior view, using visual and digital analysis, were used to assess joint space narrowing. (5) The average mean joint space loss was 0.31 mm in the placebo group and 0.07 mm in the treatment group ( $P < .05$ ; 95% confidence interval, 0.13-0.48).

The clinical relevance of knee joint space narrowing is undetermined. Radiographic evaluation of a weight-bearing joint space may not be an accurate or reproducible technique. A study of 15 patients with mild to moderate knee osteoarthritis used standing and semi-flexed radiographic views after an analgesic and nonsteroid anti-inflammatory drug washout period, and 1 to 12 weeks after resumption of analgesic therapy (mean 6.0 weeks). (6) Knee pain significantly decreased radiographic joint space in the standing anterior-posterior position, but not in the semiflexed position. Using the standing anterior-posterior method may confound accurate

interpretation of joint space narrowing and changes in articular cartilage since glucosamine may have an anti-inflammatory effect. (6)

One double-blinded randomized controlled trial, comparing chondroitin sulfate with placebo, evaluated joint space in patients with symptomatic hand osteoarthritis. (7) One hundred sixty-five Caucasian patients, aged 40 to 70 years, were randomized to receive either a 50-mg intramuscular injection of chondroitin polysulfate, twice weekly, for 8 weeks, every 4 months, versus placebo, or 400 mg of oral chondroitin sulfate, 3 times a day, versus placebo.

Osteoarthritis progression in the metacarpalphalangeal and interphalangeal joints was assessed with radiographs over 3 years. Evaluators used the Anatomic Lesion Progression Scale to assess the development of osteophytes and joint space narrowing, with or without subchondral bone changes, to determine osteoarthritis progression. This scale makes it very difficult to determine whether improvements are clinically significant.

Chondroitin sulfate and polysulfate did not prevent osteoarthritis from occurring in previously normal joints. In joints already affected, intramuscular chondroitin polysulfate significantly reduced progression of distal interphalangeal, proximal interphalangeal, and metacarpophalangeal joint space narrowing ( $P < .013$ ), using the progression scale. Oral chondroitin sulfate did not prevent progression. (7)

#### \* RECOMMENDATIONS FROM OTHERS

The American College of Rheumatology stated in 2000 that recommending glucosamine sulfate or chondroitin sulfate for osteoarthritis might be premature due to the methodology, lack of standardization, and insufficient information on study designs. More research was recommended. (8)

These products are sold as supplements in the United States. Their purity is often questionable and thus may affect study results. When studying glucosamine, the National Institutes of Health was forced to manufacture the drug itself due to lack of a reliable amount present in commercial products. (9)

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#### \* CLINICAL COMMENTARY

Most family physicians see many patients with osteoarthritis, which can be difficult to treat. My patients typically want improvement in their symptoms, traction, and disease progression. Although there is good evidence that the use of glucosamine sulphate (but not chondroitin sulphate) can improve the common symptoms and functional problems of osteoarthritis, this review states it is unclear whether these substances can alter disease progression through regeneration of cartilage.

I tell my patients with osteoarthritis that glucosamine sulfate can help problems like joint pain and function, but that we do not have a safe and reliable treatment for reversing the disease or the joint damage resulting from it.

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