

Healthy Joints™ Product Science – Glucosamine and Chondroitin

{Note: the underlined sections within the the text of the abstracts is highlighted for emphasis by us, not the authors}

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[Am Fam Physician](#). 2008 Jan 15;77(2):177-84.

Dietary supplements for osteoarthritis.

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A large number of dietary supplements are promoted to patients with osteoarthritis and as many as one third of those patients have used a supplement to treat their condition. Glucosamine-containing supplements are among the most commonly used products for osteoarthritis. Although the evidence is not entirely consistent, most research suggests that glucosamine sulfate can improve symptoms of pain related to osteoarthritis, as well as slow disease progression in patients with osteoarthritis of the knee. Chondroitin sulfate also appears to reduce osteoarthritis symptoms and is often combined with glucosamine, but there is no reliable evidence that the combination is more effective than either agent alone. S-adenosylmethionine may reduce pain but high costs and product quality issues limit its use. Several other supplements are promoted for treating osteoarthritis, such as methylsulfonylmethane, Harpagophytum procumbens (devil's claw), Curcuma longa (turmeric), and Zingiber officinale (ginger), but there is insufficient reliable evidence regarding long-term safety or effectiveness.

(2)

[Drugs Aging](#). 2007;24(7):573-80.

Glucosamine and chondroitin sulfate as therapeutic agents for knee and hip osteoarthritis.

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Osteoarthritis (OA), the most common form of arthritis, is a public health problem throughout the world. Several entities have been carefully investigated for the symptomatic and structural management of OA. This review evaluates published

studies of the effect of glucosamine salts and chondroitin sulfate preparations on the progression of knee or hip OA. Despite multiple double-blind, controlled clinical trials of the use of glucosamine and chondroitin sulfate in OA, controversy regarding the efficacy of these agents with respect to symptomatic improvement remains. Several potential confounders, including placebo response, use of prescription medicines versus over-the-counter pills or food supplements, or use of glucosamine sulfate versus glucosamine hydrochloride, may have relevance when attempting to interpret the seemingly contradictory results of different clinical trials. The National Institutes of Health-sponsored GAIT (Glucosamine/chondroitin Arthritis Intervention Trial) compared placebo, glucosamine hydrochloride, chondroitin sulfate, a combination of glucosamine and chondroitin sulfate and celecoxib in a parallel, blinded 6-month multicentre study of patients with knee OA. This trial showed that glucosamine hydrochloride and chondroitin sulfate alone or in combination did not reduce pain effectively in the overall group of patients with OA of the knee. However, exploratory analyses suggest that the combination of glucosamine hydrochloride and chondroitin sulfate may be effective in the subgroup of patients with moderate-to-severe knee pain. For decades, the traditional pharmacological management of OA has been mainly symptomatic. However, in recent years, several randomised controlled studies have assessed the structure-modifying effect of glucosamine sulfate and chondroitin sulfate using plain radiography to measure joint space narrowing over years. There is some evidence to suggest a structure-modifying effect of glucosamine sulfate and chondroitin sulfate. On the basis of the results of recent randomised controlled trials and meta-analyses, we can conclude that glucosamine sulfate (but not glucosamine hydrochloride) and chondroitin sulfate have small-to-moderate symptomatic efficacy in OA, although this is still debated. With respect to the structure-modifying effect, there is compelling evidence that glucosamine sulfate and chondroitin sulfate may interfere with progression of OA.

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[J Cosmet Dermatol](#). 2006 Dec;5(4):309-15.

Glucosamine: an ingredient with skin and other benefits.

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Both glucosamine and its derivative N-acetyl glucosamine are amino-monosaccharides that serve key biochemical functions on their own and as substrate precursors for the biosynthesis of polymers such as glycosaminoglycans (e.g., hyaluronic acid) and for the production of proteoglycans. Glucosamine has an excellent safety profile and has been shown to provide benefits in several

clinical disorders. Glucosamine compounds have been reported to have several beneficial effects on the skin or skin cells. Because of its stimulation of hyaluronic acid synthesis, glucosamine has been shown to accelerate wound healing, improve skin hydration, and decrease wrinkles. In addition, as an inhibitor of tyrosinase activation, it inhibits melanin production and is useful in treatment of disorders of hyperpigmentation. Mechanistically, glucosamine also has both anti-inflammatory and chondroprotective effects. Clinical trials have shown benefit in using oral glucosamine supplementation to improve symptoms and slow the progression of osteoarthritis in humans. Glucosamine has also been used to prevent and treat osteoarthritis in animals. Based on other observations, glucosamine has been suggested for additional clinical uses, including treatment of inflammatory bowel disease, migraine headaches, and viral infections. The current clinical uses for topical and oral glucosamine compounds and the mechanistic rationale for these uses are reviewed here.

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[Cochrane Database Syst Rev. 2005 Apr 18;\(2\):CD002946.](#)

Update of:

[Cochrane Database Syst Rev. 2001;\(1\):CD002946.](#)

Glucosamine therapy for treating osteoarthritis.

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BACKGROUND: Osteoarthritis (OA) is the most common form of arthritis, and it is often associated with significant disability and an impaired quality of life. OBJECTIVES: To review all randomized controlled trials (RCTs) evaluating the effectiveness and toxicity of glucosamine in OA. SEARCH STRATEGY: We searched MEDLINE, PREMEDLINE, EMBASE, AMED, ACP Journal Club, DARE, CDSR, and the CCTR. We also wrote letters to content experts, and hand searched reference lists of identified RCTs and pertinent review articles. All searches were updated in January 2005. SELECTION CRITERIA: Relevant studies met the following criteria: 1) RCTs evaluating the effectiveness and safety of glucosamine in OA, 2) Both placebo controlled and comparative studies were eligible, 3) Both single blinded and double blinded studies were eligible. DATA COLLECTION AND ANALYSIS: Data abstraction was performed independently by two investigators and the results were compared for degree of agreement. Gotzsche's method and a validated tool (Jadad 1996) were used to score the quality of the RCTs. Continuous outcome measures were pooled using standardized mean differences (SMD) as the

measure of effect size. Dichotomous outcome measures were pooled using relative risk ratios (RR). MAIN RESULTS: Analysis restricted to eight studies with adequate allocation concealment failed to show benefit of glucosamine for pain and WOMAC function. Collectively, the 20 analyzed RCTs found glucosamine favoured placebo with a 28% (change from baseline) improvement in pain (SMD -0.61, 95% CI -0.95, -0.28) and a 21% (change from baseline) improvement in function using the Lequesne index (SMD -0.51 95% CI -0.96, -0.05). However, the results are not uniformly positive, and the reasons for this remain unexplained. WOMAC pain, function and stiffness outcomes did not reach statistical significance. In the 10 RCTs in which the Rotta preparation of glucosamine was compared to placebo, glucosamine was found to be superior for pain (SMD -1.31, 95% CI -1.99, -0.64) and function using the Lequesne index (SMD -0.51, 95% CI -0.96, -0.05). Pooled results for pain (SMD -0.15, 95% CI -0.35, 0.05) and function using the WOMAC index (SMD 0.03, 95% CI -0.18, 0.25) in those RCTs in which a non-Rotta preparation of glucosamine was compared to placebo did not reach statistical significance. In the four RCTs in which the Rotta preparation of glucosamine was compared to an NSAID, glucosamine was superior in two, and equivalent in two. Two RCTs using the Rotta preparation showed that glucosamine was able to slow radiological progression of OA of the knee over a three year period (SMD 0.24, 95% CI 0.04, 0.43). Glucosamine was as safe as placebo in terms of the number of subjects reporting adverse reactions (RR=0.97, 95% CI, 0.88, 1.08). AUTHORS' CONCLUSIONS: This update includes 20 studies with 2570 patients. Pooled results from studies using a non-Rotta preparation or adequate allocation concealment failed to show benefit in pain and WOMAC function while those studies evaluating the Rotta preparation show that glucosamine was superior to placebo in the treatment of pain and functional impairment resulting from symptomatic OA. WOMAC outcomes of pain, stiffness and function did not show a superiority of glucosamine over placebo for both Rotta and non-Rotta preparations of glucosamine. Glucosamine was as safe as placebo.

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[Br J Gen Pract.](#) 2004 Jun;54(503):457-64.

Rheumatology and musculoskeletal medicine.

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Musculoskeletal disease accounts for a large proportion of a general practitioner's (GP's) workload. Proper management can not only improve quality of care, but also increase job satisfaction and reap rewards under the new contract. Osteoporosis creates a huge socioeconomic burden of disease and disability.

Identifying high-risk groups in primary care and using preventative treatment can result in a substantial reduction in morbidity and mortality. GPs can help by presenting a unified lifestyle message, advising on fall prevention, and providing effective treatment; in particular, calcium and vitamin D for female nursing home residents. Osteoarthritis is eminently treatable in primary care with a number of management options for GPs, in addition to drug therapy. Glucosamine and chondroitin have few side effects and are worth recommending to patients with mild knee osteoarthritis. Rheumatoid arthritis can cause significant disability, which can be limited by early diagnosis, referral, and treatment. Severe refractory rheumatoid arthritis may warrant referral for consideration of biologic therapy. Assessment of the cardiovascular risk and possible use of statins in rheumatoid patients may reduce their cardiovascular mortality. GPs should aim to help patients to achieve optimum quality of life by using a holistic approach and by allowing maximum choice and control over their disease.

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[Am Fam Physician.](#) 2003 Jan 15;67(2):339-44.

Comment in:

[Am Fam Physician.](#) 2003 Nov 1;68(9):1713; author reply 1713.

Alternative therapies for traditional disease states: osteoarthritis.

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Americans spend more on natural remedies for osteoarthritis than for any other medical condition. In treating osteoarthritis, glucosamine and chondroitin sulfate, two of the molecular building blocks found in articular cartilage, are the most commonly used alternative supplements. In randomized trials of variable quality, these compounds show efficacy in reducing symptoms, but neither has been shown to arrest progression of the disease or regenerate damaged cartilage. Although few clinical trials on S-adenosylmethionine exist, preliminary evidence indicates that it relieves pain to a degree similar to that of nonsteroidal anti-inflammatory drugs but with fewer side effects. Clinical trials of dimethyl sulfoxide offer conflicting results. Neither ginger nor cetyl myristoleate has proven clinical usefulness.

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[J Am Acad Orthop Surg.](#) 2001 Mar-Apr;9(2):71-8.

Comment in:

[J Am Acad Orthop Surg.](#) 2001 Sep-Oct;9(5):352-3.

Use of glucosamine and chondroitin sulfate in the management of osteoarthritis.

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The goals of osteoarthritis therapy are to decrease pain and to maintain or improve joint function. The pharmacologic treatment of this condition has included the use of aspirin, acetaminophen, and nonsteroidal anti-inflammatory drugs. More recently, numerous studies have investigated the potential role of chondroprotective agents in repairing articular cartilage and decelerating the degenerative process. The reports of limited clinical experience with two of these agents, glucosamine and chondroitin sulfate, as well as the accompanying publicity in the popular media, have generated controversy. Advocates of these alternative modalities cite reports of progressive and gradual decline of joint pain and tenderness, improved mobility, sustained improvement after drug withdrawal, and a lack of significant toxicity associated with short-term use of these agents. Critics point out that in the great majority of the relevant clinical trials, sample sizes were small and follow-up was short-term.

(8)

[Rheum Dis Clin North Am.](#) 1999 May;25(2):379-95.

Nutraceuticals as therapeutic agents in osteoarthritis. The role of glucosamine, chondroitin sulfate, and collagen hydrolysate.

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There are a sufficient number of short-term studies with these agents suggesting efficacy equal to that seen in the symptomatic treatment of OA using NSAIDs. Two recent meta-analyses by McAlindon and colleagues and Towheed et al reviewed clinical trials of glucosamine and chondroitin in the treatment of osteoarthritis. The study by McAlindon and co-workers included all double-blind placebo-controlled trials of greater than 4 weeks' duration, testing oral or parenteral glucosamine or chondroitin for treatment of hip or knee osteoarthritis. Thirteen trials (six with glucosamine, seven with chondroitin) met eligibility criteria. The authors used global pain score or the Lequesne index in the index joint as the primary outcome measure and considered the trial positive if improvement in the treatment group was equal to or greater than 25% compared with the placebo group, and was significant ($P < \text{or} = .05$). All 13 studies reviewed were classified as positive,

demonstrating large effects, compared with placebo (39.5% [S.D. 21.9] for glucosamine, 40.2% [S.D. 6.4] for chondroitin). The authors concluded that clinical trials of these two agents showed substantial benefit in the treatment of osteoarthritis but provided insufficient information about study design and conduct to allow definitive evaluation. Towheed and colleagues reviewed nine randomized, controlled trials of glucosamine sulfate in osteoarthritis. In seven of the randomized controlled trials, in which they compared glucosamine with placebo, glucosamine was always superior. In two randomized controlled trials comparing glucosamine to ibuprofen, glucosamine was superior in one and equivalent in one. Methodologic problems, including lack of standardized case definition of osteoarthritis and lack of standardized outcome assessment led the authors to conclude that further studies are needed to determine if route of administration is important and whether the therapeutic effect is site specific. A meta-analysis of chondroitin sulfate trials has also been published. Of the 12 published trials, 4 randomized double-blind placebo or NSAID-controlled trials with 227 patients on chondroitin sulfate were entered into the analysis. All four studies showed chondroitin sulfate to be superior to placebo, with respect to Lequesne index, visual analog scale for pain and medication consumption. Significant changes ($P < \text{or} = .05$) were seen in those treated from day 60 to the study endpoints (150 to 180 days). Pooled data demonstrated at least 50% improvement in the study variables in the chondroitin treated group. Discrepancies in some of the study findings reported in the literature may relate to the composition of the nutritional supplements used. Studies in the United States have revealed that a number of preparations claiming to contain certain doses of glucosamine or chondroitin sulfate have significantly less (or none) of the dosages described. Accordingly, it is essential that studies performed with these agents use preparations that are carefully defined in manufacture. The amounts generally administered are glucosamine, 1500 mg, and chondroitin sulfate, 1200 mg, daily. Although glucosamine has been described as effective when used alone, it is probably reasonable to use the combination pending further studies. The average cost is approximately \$30 to \$45 per month. In the interim, what should physicians tell their patients when they ask whether these agents are effective, or whether they should or should not take them? The authors emphasize that these agents are not FDA-evaluated or recommended for the treatment of OA. They are available as health food supplements, and the number of studies of toxicity, particularly with respect to long-term evaluations, is limited. The pros and cons of these agents and the published data are described so that patients can make a reasonably informed decision as to whether they wish to proceed with use of these agents in therapy.

(9)

[JAMA](#). 2000 Mar 15;283(11):1469-75.

Comment in:

ACP J Club. 2000 Sep-Oct;133(2):58.

[JAMA. 2000 Mar 15;283\(11\):1483-4.](#)

[JAMA. 2000 Sep 13;284\(10\):1241; author reply 1242.](#)

[JAMA. 2000 Sep 13;284\(10\):1241; author reply 1242.](#)

Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis.

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CONTEXT: Glucosamine and chondroitin preparations are widely touted in the lay press as remedies for osteoarthritis (OA), but uncertainty about their efficacy exists among the medical community. OBJECTIVE: To evaluate benefit of glucosamine and chondroitin preparations for OA symptoms using meta-analysis combined with systematic quality assessment of clinical trials of these preparations in knee and/or hip OA. DATA SOURCES: We searched for human clinical trials in MEDLINE (1966 to June 1999) and the Cochrane Controlled Trials Register using the terms osteoarthritis, osteoarthrosis, degenerative arthritis, glucosamine, chondroitin, and glycosaminoglycans. We also manually searched review articles, manuscripts, and supplements from rheumatology and OA journals and sought unpublished data by contacting content experts, study authors, and manufacturers of glucosamine or chondroitin. STUDY SELECTION: Studies were included if they were published or unpublished double-blind, randomized, placebo-controlled trials of 4 or more weeks' duration that tested glucosamine or chondroitin for knee or hip OA and reported extractable data on the effect of treatment on symptoms. Fifteen of 37 studies were included in the analysis. DATA EXTRACTION: Reviewers performed data extraction and scored each trial using a quality assessment instrument. We computed an effect size from the intergroup difference in mean outcome values at trial end, divided by the SD of the outcome value in the placebo group (0.2, small effect; 0.5, moderate; 0.8, large), and applied a correction factor to reduce bias. We tested for trial heterogeneity and publication bias and stratified for trial quality and size. We pooled effect sizes using a random effects model. DATA SYNTHESIS: Quality scores ranged from 12.3% to 55.4% of the maximum, with a mean (SD) of 35.5% (12%). Only 1 study described adequate allocation concealment and 2 reported an intent-to-treat analysis. Most were supported or performed by a manufacturer. Funnel plots showed significant asymmetry ($P < \text{ or } = .01$) compatible with publication bias. Tests for heterogeneity were nonsignificant after removing 1 outlier trial. The aggregated effect sizes were 0.44 (95% confidence interval [CI], 0.24-0.64) for glucosamine and 0.78 (95% CI, 0.60-0.95) for chondroitin, but they were diminished when only high-quality or large trials were considered. The effect sizes were relatively consistent for pain and functional outcomes. CONCLUSIONS: Trials of glucosamine and chondroitin preparations for OA symptoms demonstrate

moderate to large effects, but quality issues and likely publication bias suggest that these effects are exaggerated. Nevertheless, some degree of efficacy appears probable for these preparations.

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