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Abstract

An estimated 46 million adults in the U.S. are affected by arthritis, with osteoarthritis (OA) being the most common. Due to the limited pharmacologic therapy available to treat this condition, many patients are turning to dietary supplements to relieve their symptoms. Some of the most popular supplements available for the treatment of OA are glucosamine, chondroitin and methylsulfonylmethane (MSM), but many less studied products are also available. Due to limited evidence of efficacy, it is difficult to make a strong recommendation for any of these products; however, pharmacists must be able to educate the patients that choose to use these supplements in the treatment of their OA.

Introduction

Arthritis currently affects an estimated 46 million adults in the United States alone, and rates are expected to rise dramatically to 67 million over the next 20 years. It is most common in adults 65 years and older and consists of more than 100 different rheumatic diseases and conditions that impact joints, joint tissue and other connective tissue. Osteoarthritis (OA) is the most common and is defined as the degeneration of a joint's cartilage and underlying bone, leading to pain, inflammation and stiffness in the joint. Due to the high prevalence, high lifetime risk of developing OA and many other factors, this disease has become an important public health concern. It is currently the nation's leading cause of disability, causing limited activity in approximately 19 million U.S. adults. Due to the fact that it is so difficult for people to be physically active with OA, it is a high risk factor for many other chronic diseases and conditions, including obesity, diabetes and cardiovascular disease. Arthritis has been a large expense for the United States over the past several years, costing a total of \$128 billion in 2003 alone. It is the reason for approximately 992,100 hospital visits and 44 million outpatient visits every year.¹

In order to address this rising concern with arthritis, there are many counseling points that pharmacists may give to their patients affected by this disease. Advising patients to be physically active, maintain a healthy body weight, protect their joints, and schedule regular visits with a physician or even referring them to a self-management education program can be extremely beneficial.¹ The mainstay over-the-counter treatment option for relieving symptoms of OA is acetaminophen. Prescription treatment options are few, including COX-2 inhibitors, NSAIDs and even prednisone; however, these drugs do not come without their own adverse effects and risks. Often, patients with OA look to other means of easing the pain and inflammation. Supplements are becoming increasingly popular treatment options for those affected by the disease; however, patients need to be cautious when purchasing these products. Some of the most popular supplements available for the treatment of OA include glucosamine, chondroitin and methylsulfonylmethane (MSM).

Glucosamine

Glucosamine is arguably the most popular supplement used for joint health. There have been more than 20 studies performed to assess the efficacy of glucosamine alone and in combination with other supplements to treat osteoarthritis of the knee.²⁻⁶ The outcomes of these trials have been mixed; for every study performed that finds glucosamine effective, another study has been performed to find it ineffective. It is also interesting to note that many trials backed by pharmaceutical companies yielded clinically significant outcomes, whereas many independently funded trials found no clinically significant outcomes. Despite many mixed outcomes, there have been two large trials that suggest glucosamine could benefit some patient populations. The European GUIDE trial compared the efficacy of glucosamine sulfate alone (1,500 mg once daily) and acetaminophen (3,000 mg once daily) in treating osteoarthritis.⁷ The 318 enrolled patients were followed for six months, and results proved glucosamine to be more effective than acetaminophen in treating pain. The most recent American GAIT trial followed 1,500 patients for six months and then 750 of those patients for an additional 18 months. Patients were randomized to glucosamine HCL alone, chondroitin sulfate alone, glucosamine/chondroitin combination, celecoxib, or placebo.⁸ The glucosamine/chondroitin combination was the only group besides celecoxib to show significant reductions in pain, but this was only noted in the group of patients who had the most severe pain index at study onset. Interestingly, there was also a 55 percent placebo effect in this group of patients. In both cases, adverse reactions were generally mild GI effects like heartburn, diarrhea and nausea. The biggest controversy with these two trials is the use of two different glucosamine salt forms – HCL and sulfate. The GAIT trial found glucosamine HCL to be ineffective alone, but the GUIDE trial did find the sulfate form to be effective alone. The question also remains why glucosamine appears more effective in combination than as a stand-alone therapy. The place of glucosamine in current osteoarthritis patients has yet to be established, but recent studies have suggested it may have efficacy in some patient populations.

So, what do you tell a patient who is interested in using glucosamine? First, explain that efficacy has only been established in certain patient populations, and it may or may not be right for them. Next, you need to inform your patient that the only form that has been proven efficacious is the oral sulfate form. The sulfate form is typically more expensive (anywhere from \$9 to \$32 for a one-month supply) because it is more costly to manufacture.⁹ Glucosamine is expensive regardless, but you want to make sure your patient gets the most effective product for their money. Do not recommend glucosamine cream because efficacy has not been established. At least 1,500 mg daily is needed to be beneficial, and this dose is often broken up into BID or TID dosing. Research has also proven that glucosamine must be used for a minimum of 30 to 90 days to notice any effect.¹⁰ Encourage the patient to try at least a 60-day trial period before making the decision to continue or discontinue therapy.

Chondroitin sulfate

Chondroitin, found naturally in the human body, is marketed as a cartilage matrix enhancer that helps rebuild and prevent the breakdown of cartilage, thereby maintaining healthy joint function.¹¹ In the body, it is a major component of connective tissue and joint cartilage, and its ability to absorb water increases cartilage thickness and its capacity to tolerate the impact of compressive forces. Additionally, it inhibits synovial enzymes, such as elastase and hyaluronidase, which are thought to destroy cartilage and, thus, weaken joints. Synthesis of chondroitin decreases with age.¹²

Chondroitin is one of the most common over-the-counter supplements that patients buy in an effort to improve their joint health, yet clinical evidence supporting its effectiveness is limited and inconsistent. The earliest trials that demonstrated its efficacy were not of high quality.¹³ More recent and superior-quality studies show that chondroitin does not reduce the pain associated with OA. While chondroitin most likely does not have a place in OA therapy for symptom relief, current research has examined its place in structural management of OA. Because of its structure-modifying effect, chondroitin may slow OA progression.¹⁴ A meta-analysis examined this beneficial effect in patients with knee OA and determined that it did have a significant protective effect on joint narrowing space, but only after two years of daily treatment. Furthermore, this study also showed that chondroitin may slow the radiological progression of OA with prolonged daily treatment.¹⁵

A normal dose of chondroitin is 200-400 mg two to three times per day, or 800-1,200 mg once daily, most often in combination with glucosamine and other supplements. These combination products usually come as a 60-day supply (120 count, taken twice daily), and prices range from \$19.99-\$47.99, depending on the number of ingredients and the relative milligram strength of each. There are also many dosage forms available, including tablets, capsules, softgels, drinks and flavored powder packets to add to water.¹⁶

Due to insufficient quality clinical evidence supporting its effectiveness, lack of symptom relief and high cost, chondroitin should not be recommended to patients. Further studies need to be performed to determine if the structure-modifying effect does slow the progression of OA and if this can be associated with any clinically significant outcomes for patients, such as improved quality of life.

MSM

MSM is an organic compound found in green plants, certain species of algae, fruits, vegetables, grains, bovines and humans. It is the oxidized metabolite of dimethylsulfoxide (DMSO) and is commercially produced by combining DMSO with hydrogen peroxide. Preliminary research suggests it might inhibit the degenerative changes in joints, thus helping with pain and swelling and possibly improving joint or physical function.¹⁷ This might be due to the compound's ability to increase blood flow, reduce muscle spasms and inhibit type C nerve fibers from transmitting pain impulses and its power to limit the release of inflammatory mediators. The sulfur present in MSM also is an important element in proteins, connective tissues, hormones and enzymes and, therefore, is significant in the formation of cartilage.¹⁸ MSM has been shown to be safe when taken orally in amounts up to 6 g per day for three months, but safety

when used topically or in pregnancy has not yet been established. Adverse effects include nausea, diarrhea, bloating, headache, fatigue, insomnia and difficulty concentrating; however, these effects have not been very prevalent. Additional side effects in some patients include pruritus and enhanced allergy symptoms. In the treatment of osteoarthritis, MSM should be taken as 500 mg three times daily up to 3 g twice daily.¹⁷ A 30-day supply of 1,500 mg MSM tablets can cost anywhere from \$10 to \$20.¹⁹

A randomized, double-blind, placebo-controlled pilot clinical trial was conducted to evaluate the efficacy of MSM in the treatment of osteoarthritis pain in the knee. Fifty patients were given either placebo (n=25) or 3 g of MSM twice daily (n=25) and were evaluated for 12 weeks. Primary outcome parameters were evaluated using the Western Ontario and McMaster University Osteoarthritis Index VAS (WOMAC), which included pain, stiffness, physical function and aggregated total symptoms. Secondary parameters included patient and physician global assessments (disease status and response to therapy) and overall health-related quality of life. Of the 40 patients who completed the study, the MSM group was found to have a significant reduction in WOMAC pain and impairment of physical function ($p<0.05$). MSM also was found to significantly improve the performance of activities of daily living compared to placebo ($p<0.05$). There was not a significant change in stiffness or aggregated total symptoms. Even though there was a statistically significant improvement in pain and physical function, the small difference in comparison to the placebo group indicates little clinical significance. Researchers also state that, although few adverse events were noted, the long-term benefits and safety cannot be determined from this trial and more studies need to be conducted.²⁰

On the other hand, another randomized, double-blind, parallel, controlled clinical trial that assessed the efficacy of glucosamine, MSM, and their combination in osteoarthritis did find significantly positive clinical findings. A total of 118 patients received either 500 mg glucosamine, 500 mg MSM, glucosamine and MSM, or placebo three times daily for 12 weeks. Pain, swelling, the Lequesne index (assessed pain or discomfort, maximum distance walked and activities of daily living) and use of rescue medication were all evaluated as outcome parameters. After 12 weeks of therapy, MSM alone was found to significantly decrease the pain and swelling index from 1.53 ± 0.51 to 0.74 ± 0.65 ($p<0.001$) with the combination product producing even greater effects. The glucosamine/MSM combination also demonstrated a significant reduction in the Lequesne index ($p<0.001$). Overall, MSM alone and in combination with glucosamine were found to demonstrate significant analgesic and anti-inflammatory actions in the treatment of osteoarthritis.²¹

Due to the conflicting evidence regarding efficacy and the unknown safety of MSM, more studies need to be conducted. Any patients taking this supplement in the long-term treatment of osteoarthritis should consult a physician before beginning use.

Other Products

There are numerous other products and therapies thought to have a benefit in OA. The table below discusses some of the more popular ones, including their possible benefit and presumed effectiveness, based on limited clinical evidence:¹³

Product	Possible Benefit	Effectiveness
SAME	Comparable to celecoxib/ other NSAIDS for decreasing OA symptoms with fewer side effects. May require longer treatment period.	Likely effective
Avocado/soybean	Improves pain, overall disability	Possibly effective
Beta-carotene	Slows progression, not development of disease	Possibly effective
Camphor (topical)	Symptom relief through counterirritant effects	Effective
Niacin (Vitamin B3)	Improves joint flexibility and reduces inflammation	Possibly effective
Vitamin C	Reduces risk of cartilage loss and disease progression	Possibly effective
Vitamin E	No decrease in symptoms, slows cartilage loss, reduces risk of disease development	Probably ineffective
Insufficient evidence: DMSO, gelatin, ginger, vitamin B5, selenium Nonpharmacologic treatment: acupuncture, mineral baths, magnet therapy, yoga		

OTC Regulation

The lax regulations surrounding dietary supplements are an important counseling point for all patients. The Dietary Supplement Health and Education Act (DSHEA) of 1994 mandated that the dietary supplement manufacturer is responsible for product safety, not the Food and Drug Administration (FDA).²² Manufacturers do not need to register their products with the FDA before marketing, and the FDA can only withdraw a product from the market after multiple serious adverse drug reactions (ADRs) have occurred. Some companies choose to undergo investigation and certification through paid outside sources, but this is not mandatory.²³ The FDA can post lists of dietary supplements that may contain harmful ingredients but can only pull these products off the market after there have been multiple documented cases of serious ADRs (usually death).²⁴ Encourage patients to research the product manufacturer before buying their dietary supplements.

Conclusion

Osteoarthritis affects 46 million Americans and is the leading cause of disability.¹ As America ages, many are looking for ways to prevent problems or treat existing problems without prescription medication. Glucosamine is likely to be efficacious, but patients must be careful of which type they buy. MSM and chondroitin lack strong evidence for use at present, and MSM has yet to prove safety, so patients should talk to their doctor prior to starting therapy. At this time, there is a definite lack of evidence proving success or failure for many natural products on the market; however, as health care professionals, it is our responsibility to educate our patients when more evidence has been brought to light about the herbal products they may be taking.

Resources

1. Arthritis: Meeting the Challenge: At a Glance 2010 [website on the Internet]. Atlanta (GA): Centers for Disease Control and Prevention; [updated 2010 Jan 28; cited 2010 Mar 21]. Chronic Disease Prevention and Health Promotion Publications; [about 10 screens]. Available at www.cdc.gov/chronicdisease/resources/publications/aag/arthritis.htm.

2. McAlindon T, LaValley M, Gulin J, Felson D. Glucosamine and chondroitin for treatment of osteoarthritis. *JAMA* 2000;283:1469-75.
3. Hughes R, Carr A. A randomized, double-blind, placebo-controlled trial of glucosamine sulphate as an analgesic in osteoarthritis of the knee. *Rheumatology* 2002;41:279-84.
4. Pavelka K, Gatterova J, Olejarova M, Machacek S, Giacovelli G, Rovati L. Glucosamine sulfate use and delay of progression of knee osteoarthritis. *Arch Intern Med* 2002;162: 2113-23.
5. Cibere J, Kopec J, Thorne A, Singer J, Carvin J, Robinson D, et al. Randomized, double-blind, placebo-controlled glucosamine discontinuation trial in knee osteoarthritis. *American College of Rheumatology* 2004;51:738-45.
6. Herrero-Beumont G, Ivorra J, Trabado M, Blanco F, Benito P, Martin-Mola E, et al. Glucosamine sulfate in the treatment of knee osteoarthritis symptoms: a randomized, double-blind, placebo-controlled study using acetaminophen as a side comparator. *American College of Rheumatology* 2007;56:555-67.
7. Herrero-Beumont G, Román JA, Trabado MC, Blanco FJ, Benito P, Martin-Mola E, 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 [abstract]. *Arthritis Rheum* 2005;9 Suppl:1203.
8. Sawitzke A, Shi H, Finco M, Dunlop D, Bingham C, Harris C, et al. The effect of glucosamine and/or chondroitin sulfate on the progression of knee osteoarthritis: a report from the glucosamine/chondroitin arthritis intervention trial. *American College of Rheumatology* 2008; 58(10):3183-91.
9. Glucosamine. Drugstore.com. [cited 2010 Apr 1]. Available at www.drugstore.com.
10. Dahmer S, Schiller R. Glucosamine. *Am Fam Physician* 2008;78(4): 471-6, 481.
11. Chondroitin; Glucosamine [monograph on the internet]. *Clinical Pharmacology* [cited 2010 Mar 20] Available at 0-www.clinicalpharmacology-ip.com.
12. Chondroitin sulfate.[monograph on the internet]. Lexi-Comp Online. Lexi-Comp, Inc. [cited 2010 Apr 1] Available at online.lexi.com/crisql/servlet/crlonline.
13. Osteoarthritis. Natural Medicines Comprehensive Database. [cited 2010 Mar 20]. Available from www.naturaldatabase.com.
14. Bruyere O, Reginster JY. Glucosamine and chondroitin sulfate as therapeutic agents for knee and hip osteoarthritis. *Drugs Aging* 2007;24:573-80.
15. Lee YH, Woo JH, Choi SJ, Ji JD, Song GG. Effect of glucosamine or chondroitin sulfate on the osteoarthritis progression: a meta-analysis. *Rheumatol Int* 2010;30:357-63.
16. Chondroitin. Drugstore.com. [cited 2010 Apr 1]. Available at www.drugstore.com.
17. MSM [monograph on the Internet]. Stockton (CA): Natural Medicines Comprehensive Database; 2010 [cited 2010 Mar 21]. Available at www.naturaldatabase.com.
18. Natural Products Database [database on the Internet]. Hudson (OH): Lexi-Comp ONLINE. 2010 [cited 2010 Mar 21]. Available at online.lexi.com/crisql/servlet/crlonline.
19. Drugstore.com. Drug Prices & Information. Available at www.drugstore.com/search/search_results.asp?Ntt=MSM&Ntx=mode%2bmatchallpart.
20. Kim LS, Axelrod LJ, Howard P, Buratovich N, Waters RF. Efficacy of methylsulfonylmethane (MSM) in osteoarthritis pain of the knee: a pilot clinical trial. *Osteoarthritis Cartilage* 2006;14:286-294.
21. Usha PR and Naidu MUR. Randomised, double-blind, parallel, placebo-controlled study of oral glucosamine, methylsulfonylmethane and their combination in osteoarthritis. *Clin Drug Investig* 2004;24(6):353-63.
22. Segal A. CHPA regulation of over-the-counter-medicines. 2009.
23. Dietary supplements. FDA. Available at www.fda.gov/food/DietarySupplements/default.htm.
24. Using dietary supplements wisely. NCCAM. 2009. Available at nccam.nih.gov/health/supplements/wisewise.htm.