



REVIEW I-Flex and Management of Inflammation in Osteoarthritis

Tammy Wolhuter, RD (SA) & Anne Till, RD(SA)

From: Anne Till & Associates, Registered Dietitians

1. Introduction

Osteoarthritis (OA) is a chronic joint disease that involves the loss of habitually weight-bearing joint cartilage. OA may occur in any synovial joint in the body, although the condition is most common in hands, knees, hips and spine [1]. The loss can result in pain, swelling, loss of motion, changes in joint shape and abnormal bone growth [2]. Inflammatory processes are involved, leading to stiffness and pain [3]. OA occurs through hereditary factors and trauma. Mechanical insult may lead to the appearance of the disease at a particular site. Obesity plays a role in the occurrence and progression of the disease [4]. Since obese individuals have higher concentrations of inflammatory markers, inflammation may contribute to functional limitation and disease progression in those who have OA [5].

2. Mechanisms Contributing to Pain in OA

Inflammation in the synovial joints play a role in the pathogenesis of pain experienced in patients with OA [4]. Inflammatory mediators can affect muscle function and lower pain threshold, thus worsening the pain experienced in OA [5]. The severity, mobility, pain and stiffness are partly mediated by the level of chronic inflammation in a patient with OA. Diffusion of cytokines from the synovial fluid into the cartilage could contribute to the cartilage matrix loss observed in OA by stimulating chondrocyte catabolic activity and inhibiting anabolic activity [5].

3. Treatment of OA

Lifestyle modification, particularly exercise and weight reduction, is a core component of the management of OA. Non-loading activities such as swimming and weight-bearing exercises have been shown to reduce symptoms, increase mobility and reduce continuing damage from OA [2]. A knowledgeable physical or occupational therapist can teach patients how to exercise safely and how to protect joints while doing routine activities of daily living. Weight loss reduces OA-associated pain and improves physical activity [11] [4]. Weight loss reduces risk factors for symptomatic knee OA and reduces pro-inflammatory cytokines and adipokines believed to play a role in cartilage degradation [5]. Pharmacological treatment of OA includes analgesics and non-steroidal anti-inflammatory drugs (NSAIDs) [4]. Paracetamol is the oral analgesic of first choice and the preferred long-term analgesic, if successful. However, NSAIDs must be considered in patients with no response to paracetamol. NSAIDs are often associated with adverse side effects, such as nausea, epigastric pain or even peptic ulcers [3], which can be life threatening in the elderly [10]. Safer therapies are therefore required [10].

4.1 Supplements for OA

There are a number of supplements or preparations available aimed at reducing pain and inflammation in the joints which are associated with arthritic conditions. The formulation for each supplement varies considerably according to manufacturer specifications. Most frequently used supplements include glucosamine, chondroitin, methylsulfonylmethane (MSM) S-adenosylmethionine (SAMe), copper, manganese, iron, zinc, boron, vitamin C, omega-3 fatty acids, beta-carotene, vitamin E and selenium, and more recently rose hips. Not all of these supplements will be discussed in detail in this particular review.

4.1.1 Glucosamine and Chondroitin

Glucosamine and chondroitin are essential components of the proteoglycan in normal cartilage, which is the main reason for their use as supplements in the management of OA.

Glucosamine is used as an agent to help relieve the symptoms and delay the progression of OA. It is hypothesized that OA is associated with a local deficiency in some key natural substances and that glucosamine might act as a substrate for cartilage repair, by stimulating proteoglycan synthesis by chondrocytes [3]. Glucosamine is a slow-acting substance as treatment is usually characterized by several weeks delay in the onset of improvement in symptoms of OA [3]. A dietary supplement of glucosamine is derived from marine exoskeletons, such as shellfish or crab shells. Those who are allergic to shellfish should naturally avoid the use of glucosamine in the form of shellfish. Synthetic glucosamine is also available [3]. Occasional side effects which occur with the use of glucosamine are gastrointestinal, including abdominal pain, diarrhea, heartburn, nausea, epigastric pain and flatulence [3].

Chondroitin is an important component for the structural and functional integrity of the joints as it constitutes the majority of glycosaminoglycans in articular cartilage. Chondroitin helps maintain the viscosity in joints, stimulates cartilage repair and inhibits enzymes that degrade cartilage. These properties may result in pain relief and improved joint mobility in patients with OA as well as a reduced rate of joint destruction [3]. A dietary supplement of chondroitin is produced from animal sources, such as bovine trachea or shark cartilage [3]. Gastrointestinal side effects may be experienced with the use of chondroitin [3].

The use of glucosamine in conjunction with chondroitin is believed to be more effective compared to each used in isolation [3]. The combination of these two compounds bridges the symptomatic and preventative approach since they may have the ability to maintain and rebuild cartilage, reduce joint pain and reduce the progression of joint degeneration [3]. These treatments are easily available, better tolerated and safer to use compared to anti-inflammatory drugs [3]. However, further well-designed trials are necessary to confirm their short- and long-term efficacy in OA [3].

It is important to note that most supplements do not contain the high levels of both glucosamine and chondroitin as per the scientific literature.

4.1.2. Rose Hip as a Supplement for OA

Herbal anti-inflammatory medicines have been researched over the years as an alternative treatment for OA. *Rosa canina* (or rose hip) has attracted particular interest for its possible pain alleviating properties. Various preparations and isolated constituents from rose hip and rose hip seed have been studied in a variety of *in vitro* (experimentation performed in a controlled environment outside of a living organism) and *in vivo* (experimentation using a whole organism) tests. In a randomized, double-blind, placebo controlled trial done by Winther et al., (2005) it was found that joint pain and stiffness was significantly reduced within 3 weeks of initiating a supplement of rose-hip powder. During the course of the 3-month treatment period in which patients received active treatment, there was a significant reduction in the consumption of traditional painkillers such as paracetamol. The powder was seen to be well tolerated without any adverse side effects. This study indicated that C-reactive protein, as well as the cellular production of neutrophil leucocytes, were decreased when using concentrations of rose-hip powder. *Therefore, one mode of action of rose-hip powder might be an anti-inflammatory action mediated by leucocyte neutrophils* [11]. In two systematic reviews done in 2006 and 2008 by Chrubasik, et al., it was concluded that although evidence of the effectiveness is only moderate for OA, there is a *proven overall antioxidative, anti-inflammatory effect and analgesic potential of rose hip* [12] [10]. Rose hip powder seems to have a consistent, small to moderate efficacy on pain in OA patients. Rose hip has been shown to reduce pain and the feeling of discomfort in patients with OA. However, an efficacy is only observed in short-term clinical trials. Further large-scale clinical trials need to be done to research the efficacy of this product. Further research is required to determine the optimal dose, test the long-term treatment and compare with the impact of NSAIDs, and evaluate the biological activity of different sub-types of rose-hip. Rose hip can be used as a supplement to help relieve pain in OA, but not as treatment for OA.

4.1.3 Comparison of clinical study outcomes & characteristics of Rosehip powder v. Glucosamine HCl+Chondroitin

	Rosehip powder	glucosamine HCl + chondroitin (GAIT study) ¹
Speed of action	3 weeks ²	6 months
Efficacious in mild to mod. OA	Yes ^{2,3}	No
Efficacious in mod. to severe OA	Yes ⁴	Yes
Reduction in rescue meds	Yes ^{2,3}	No
Plant based	Yes – <i>Rosa canina</i> (i.e. wild dog rose)	No glucosamine – shellfish chondroitin – animal cartilage
Product Form	2 piece vegetarian hard-shell easily digested	Tablets more difficult to break down
Side Effects	None different from placebo	None different from placebo
Major Food Allergens	None	Yes – shellfish
Patented ingredient	Yes	No
Branded ingredient	Yes	No

1—Clegg et al GAIT NIH Study (2006); 2 –Winther et al (2005); 3—Rein et al (2004); 4—Warholm et al (2003)

4.1.4 I-Flex Nutrition Information

	Per Capsule	Per daily Dose
Rosehip powder (<i>Rosa canina</i>)	750 mg	4500 mg

5. Conclusion

Clinical evidence suggests that inflammatory processes linked to free radical generation resulting in oxidative stress may be the key in the generation of osteoarthritis. To optimize the treatment of these patients, it is necessary to understand the root cause of oxidative stress. Excess nourishment, combined with a sedentary lifestyle, results in an over abundance of glucose and fatty acid accumulation within muscle, adipose tissue and pancreatic cells. This leads to the generation of excess reactive oxygen species through the mitochondrial electron-transport chain, and inflammation.

The importance of a healthy lifestyle remains the core component of preventing and managing chronic disease. Abstaining from smoking, regular physical activity and modest (if any) intake of alcohol, a diet low in inflammation-inducing molecules, saturated and trans fatty acids, sugar and refined carbohydrates; and high in anti-inflammatory molecules, n-3 fatty acids, plant fibres, vitamins and antioxidants found in fruit and vegetables, is effective in supporting optimal ageing and reducing the incidence of chronic diseases [13]. Certain supplements may be useful in reducing the inflammatory process and may be considered as an adjunct to a healthy lifestyle. However, further studies are required to prove clinical effectiveness for certain supplements.

Reference:

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