

Review Article

Potential use of glucosamine, chondroitine, chitosan and phytoestrogen for patients with osteoarthritis

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ABSTRACT

The burden of musculoskeletal disease has increased significantly to become the second leading cause of YLD (years of life with disability). Osteoarthritis (OA) therapy that is often given is ibuprofen (NSAID) often give side effects. Therefore, it is necessary to conduct a literature review to explore evidence of how much potential these materials have for treating OA. The literature review was conducted on four databases, e.g., Pubmed, Scopus, Science direct, Clinical Key. We used several keywords to find each topic of discussion. Topic 1, benefits of glucosamine chondroitine; topic 2, benefits of chitosan; topic 3, benefits of phytoestrogens. Data from included studies were then extracted. Obtained data were analyzed using descriptive statistical methods. Glucosamine-chondroitin had a significant effect in reducing pain, reducing inflammation, reducing the rate of joint space narrowing and helping to improve joint function in OA patients with long-term use. Furthermore, the potential of chitosan can help bone remodeling, reduce pain, and inflammation. Besides, phytoestrogens also have the potential to increase bone mineral density, reducing the rate of bone turnover and reduce the occurrence of obesity through its anti-cholesterol effects. The complexity of the mechanism of action given, ranging from preventing the biggest risk factor, namely obesity; treating the main causes such as inflammation and cartilage damage; and also to treating the symptoms such as joint pain and stiffness. In the future, it is necessary to conduct clinical trials study using the ingredients glucosamine, chondroitin, chitosan and phytoestrogens to treat patients with OA.

Keywords: Osteoarthritis therapy, Joint arthritis, Joint inflammation therapy

INTRODUCTION

The burden of musculoskeletal disease has increased significantly to become the second leading cause of YLD (years of life with disability). In 2015 YLD's largest contribution among musculoskeletal disorders was due to back and neck pain, followed by OA. OA, contributed about 7.1% of this burden and showed a statistically significant improvement.

Between 1990 and 2007 there was a statistically significant 63.1% increase in the YLD burden due to OA.¹ OA therapy that is often given is ibuprofen (NSAID). Ibuprofen can cause ulceration in the patient's stomach or intestines, especially if the patient takes it for a long time or in large doses.^{1,6}

Therefore, the authors tried to find a formula from natural ingredients to deal with the problem of OA, so that the side effects of the drug can be reduced to a minimum.

Shrimp shell contains glycosamine chondroitine which functions as an anti-inflammatory and chitosan which acts to replace damaged tissue. Soybeans (glycine max) contain phytoestrogens that can maintain bone strength. With the right formulation containing these ingredients, it is possible to find herbal ingredients for the treatment of OA. Therefore, it was necessary to conduct a literature review to explore evidence of how much potential these materials have for treating OA.²

Search strategy

The literature review was conducted on four databases, e.g., Pubmed, Scopus, Science direct, Clinical Key.

We used several keywords to find each topic of discussion. topic 1, benefits of glucosamine chondroitine; keywords: glucosamine chondroitine and (bone or inflammation or chondrocyte or cartilage or joint or osteoarthritis or regeneration or pain); topic 2, benefits of chitosan. keywords: chitosan and (bone or inflammation or chondrocyte or cartilage or joint or osteoarthritis or regeneration or pain); topic 3, benefits of phytoestrogens. keywords: phytoestrogen and (bone or inflammation or chondrocyte or cartilage or joint or osteoarthritis or regeneration or pain or obese or cholesterol).

Study selection

Studies included into this study must fulfil several inclusion criteria. They should discuss the potential benefit of glucosamine chondroitine or chitosan or phytoestrogen for OA treatment; written in English; using at least *in vitro* method; and published no later than 15 years ago. The study will be excluded if the full text of the study is inaccessible.

Data analysis technique

Data from included studies were then extracted. Obtained data were analyzed using descriptive statistical methods. After that, the data collected from the three topics will be combined and conclusions will be drawn about the potential use of glucosamine chondroitin, chitosan and phytoestrogens as options for osteoarthritis therapy.

Location, time and duration of activities

The literature search was conducted in August 2022.

Topic 1: Benefits of glucosamine chondroitine

From the articles searching, authors found five articles that discussed the benefits of glucosamine chondroitine in the treatment of osteoarthritis patients.

The first study showed that chondroitin and glucosamine were as effective as celecoxib in reducing joint pain, stiffness, joint swelling and limitation of joint function in osteoarthritis patients after 6 months of treatment with

very few side effects.² A second study using a fixed-dose combination of glucosamine and chondroitin showed that glucosamine and chondroitin were not inferior to drugs used for symptomatic relief of OA with high drug tolerance.³ The third study found that the combination of glucosamine and chondroitin was able to reduce the rate of joint narrowing and pain in OA patients.⁴ The fourth study showed that dietary supplementation using glucosamine and chondroitin was able to reduce pain and improve mobility function of OA patients after 6 months of use.⁵ The fifth study showed that short-term (2 months) glucosamine and chondroitin supplementation did not effectively reduce joint pain in OA patients.⁶

From the collected studies, it can be seen that glucosamine-chondroitin has a significant effect in reducing pain, reducing inflammation, reducing the rate of joint space narrowing and helping to improve joint function in OA patients with long-term use.

Topic 2: Benefits of chitosan

From the articles searching, authors found two articles that discussed the benefits of chitosan in the treatment of osteoarthritis patients.

The first article showed that chitosan was able to accelerate bone remodeling in experimental animals, clinical bone repair occurred on day 15 and histological improvement occurred on day 16.⁷

The second article found that topical application of chitosan was able to reduce signs of inflammation and postoperative pain.⁸

Not many studies have discussed the benefits of chitosan in OA. However, the potential of chitosan for the treatment of OA is very convincing because chitosan can help bone remodeling, reduce pain, and inflammation.

Topic 3: Benefit of phytoestrogens

From the articles searching, authors found four articles that discussed the benefits of phytoestrogens in the treatment of osteoarthritis patients.

The first article showed that phytoestrogens were able to significantly lower total cholesterol and reduce bone turnover rates.⁹ The second study showed that phytoestrogen supplementation was able to increase bone mineral density of postmenopausal women after twenty-four months of supplementation.¹⁰ A third study showed that phytoestrogens derived from *Epimedium brevicornum* maxim exert a beneficial effect in preventing bone loss in late postmenopausal women without causing endometrial hyperplasia.¹¹ The third study showed that adult mice fed with a soy-rich diet had reduced body weight, adiposity and resistance to cold. This result showed that phytoestrogens feeding could be used to treat obesity.¹²

For this topic, the authors set a minimum time limit for articles that can be published 15 years ago, due to the lack of research exploring phytoestrogens recently. However, from previous studies, phytoestrogens have the potential to be used as a therapeutic option for OA among them are helping to increase bone mineral density, reducing the rate of bone turnover and helping to reduce the occurrence of obesity through its anti-cholesterol effects.

DISCUSSION

Potential benefit of combined formula from glucosamine, chondroitin, chitosan, and phytoestrogens to treat OA

Glycosamine and chondroitin have major anti-inflammatory and analgesic roles. Chitosan has a key role in the regeneration of damaged tissue. While phytoestrogens have a major role in maintaining bone mineral density and preventing obesity.^{1,12}

OA arises from the failure of chondrocytes to maintain a balance between synthesis and degradation of the extracellular matrix.¹³ Inflammatory activity causes an increase in degradation enzymes that leave debris which in turn causes ongoing inflammation. Furthermore, this will result in continuous degradation of the cartilage.¹⁴

The main symptom of osteoarthritis is pain and stiffness in the joints. This can cause difficulty in moving and performing certain activities. These symptoms can appear in only a few episodes related to activity or weather, or in severe cases they can appear continuously (NHS, 2019).¹⁵

Obesity is the greatest modifiable risk factor for OA. Subjects with a BMI >30 kg/m² had 6.8 times the chance of developing OA.¹⁷ Therefore, to prevent the occurrence and worsening of OA is very important to overcome the problem of obesity in patients.

CONCLUSION

After conducting this literature review study, the combination of glucosamine, chondroitin, chitosan, and phytoestrogens is very suitable to treat OA cases. The complexity of the mechanism of action given, ranging from preventing the biggest risk factor, namely obesity; treating the main causes such as inflammation and cartilage damage; and also, to treating the symptoms such as joint pain and stiffness. Therefore, in the future it is necessary to conduct clinical trials study using the ingredients glucosamine, chondroitin, chitosan and phytoestrogens to treat patients with OA.

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