

LITERATURE REVIEW ON GLUCOSAMINE AND CHONDROITIN IN OSTEOARTHRITIS TREATMENT

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Osteoarthritis is a chronic disease primarily characterized by articular cartilage damage. In Vietnam, osteoarthritis accounts for a high percentage of musculoskeletal conditions, especially affecting the knee joints. Recently, slow-acting anti-osteoarthritis drugs, including glucosamine, chondroitin sulfate, and diacerein, have been suggested as key pharmacological options for treating this condition. However, Vietnamese-language resources on these active ingredients remain limited. This article provides a literature review on the efficacy and safety of these drugs to enhance their effective use in clinical practice. Results indicate that glucosamine and chondroitin are both effective and safe for osteoarthritis treatment, as demonstrated by the data analyzed in this study.

Keywords: Glucosamine; chondroitin; osteoarthritis.

1. Introduction

Osteoarthritis is a chronic disease that mainly affects articular cartilage, along with the subchondral bone, ligaments, synovial membrane, and surrounding muscles [1]. This condition is highly prevalent worldwide. In the United States, approximately 21 million people suffer from osteoarthritis each year, with 4 million hospitalizations and about 100,000 cases of severe knee osteoarthritis leading to mobility issues [2]. Osteoarthritis is the second leading cause of disability in the elderly, following cardiovascular disease [3]. In Vietnam, although exact statistics are unavailable, osteoarthritis constitutes a significant portion of musculoskeletal diseases, particularly in the knee joints [4].

Non-drug treatments such as physical therapy, including infrared radiation, hot compresses, mineral baths, and mud packs, are generally simple and low-risk but yield limited effectiveness. Painkillers and non-steroidal anti-inflammatory drugs (NSAIDs) offer quick relief but often lead to severe complications like peptic ulcers, gastrointestinal bleeding, hypertension, and liver and kidney damage, with some cases proving fatal. Corticosteroid injections provide rapid symptom relief in

knee osteoarthritis; however, long-term use can lead to articular cartilage degradation and local complications like drug-induced arthritis or infections [5], [6].

Injections of hyaluronic acid (a lubricant) can restore joint lubrication and shock absorption functions. However, studies suggest that this treatment does not consistently yield long-term benefits or protect and regenerate articular cartilage [7], [8]. Surgical interventions are typically reserved for advanced stages or anatomical changes in the joint and are often costly for patients.

Recently, slow-acting anti-osteoarthritis drugs (SYSADOA), including glucosamine, chondroitin sulfate, diacerein, avocado/soybean unsaponifiables (ASU), and hyaluronic acid, have been proposed as a first-line pharmacological option for long-term symptom control in osteoarthritis. However, Vietnamese-language literature on these active ingredients remains limited. Thus, we undertook this article to review the mechanisms, efficacy, and safety of these drugs, aiming to improve their use in clinical practice.

2. Research subjects and methods

2.1. Research subjects

Articles discussing glucosamine and chondroitin's mechanism, effectiveness, and safety in osteoarthritis treatment were included if they met the selection criteria. Only articles published on PubMed from January 1, 2019, to January 1, 2024, with full-text access were considered. Abstracts and posters were excluded.

2.2. Methods

Systemic review methods have been applied.

2.3. Database

A systematic search was conducted on PubMed using the following terms: (“glucosamine” OR “glucosamine hydrochloride” OR “glucosamine sulfate” AND “osteoarthritis”); (“chondroitin” OR “chondroitin sulfate” AND “osteoarthritis”).

3. Results

After completing the search outlined in section 2.3, we identified 25 articles related to glucosamine and chondroitin. Following a full-text review, we selected:

- **Glucosamine:** 2 articles on its mechanism and 4 on its efficacy and safety.
- **Chondroitin:** 4 articles on its mechanism and 2 on its efficacy and safety.

Each article was examined for study design, sample size, and findings concerning the mechanism, efficacy, or safety of glucosamine and chondroitin.

Table 1: *Summary of article information*

Lead Author	Year	Design study	Intervention group	Sample size	Results	Ref.
Olivier Bruyère	(2016)	Survey	Glucosamin sulfate and chondroitin sulfate	600 patients	Mechanism	[9]

Lead Author	Year	Design study	Intervention group	Sample size	Results	Ref.
Hiba Murtadha Al-Saadi	(2019)	Randomized, double-blind, controlled trial	Glucosamin sulfate	32 patients	Mechanism	[10]
Lomonte	(2019)	Multicenter, randomized, double-blind study	Glucosamin sulfate	100 patients	Effective and safe	[11]
Lomonte	(2021)	Multicenter, randomized, single-blind clinical trial	Glucosamine sulfate and chondroitin sulfate	627 patients	Effective and safe	[12]
Muhammad Salman	(2022)	Randomized, controlled trial	Glucosamin Sulfate/ Chondroitin sulfate combined physical therapy	30 patients	Effective and safe	[13]
Akifumi Tsuruta	(2018)	Randomized, double-blind, controlled trial	Glucosamine	41 patients	Effective and safe	[14]
H. C. Hsu	(2022)	Invitro	Chondroitin sulfate	Chon-001 cells were seeded into 24-well culture plates at a density of 1×10^5 cells/well	Mechanism	[15]
Xiang Li	(2021)	Experiment on animals	Chondroitin sulfate - semi5	18 mice	Mechanism	[16]
Sevimli	(2021)	Experiment on animals	Chondroitin sulfate	40 rabbits	Mechanism	[17]
Zhenkun Ren	(2018)	Experiment on animals	Chondroitin sulfate	24 male mice	Mechanism	[18]
Sadykov	(2020)	Randomized, controlled trial	Chondroitin sulfate	70 patients	Effective	[19]
Rondanelli	(2020)	Randomized, double-blind, controlled trial	Chondroitin sulfate	48 patients	Effective	[20]

Comments: Most safety and efficacy studies are randomized controlled clinical trials of high significance.

3.1. Glucosamine

3.1.1. Definition

Glucosamine is a water-soluble monosaccharide consisting of a glucose molecule attached to an amino group. It is derived from the hydrolysis of chitin or chitosan and is a derivative of glucose metabolism in cells, where the hydroxyl group at position 2 is replaced by an amino group. The primary exogenous source of glucosamine is the exoskeleton of crustaceans. In dietary supplements, glucosamine exists in several forms, including glucosamine sulfate (GS), glucosamine hydrochloride (GH) (without the sulfate group), and crystalline glucosamine sulfate. GS requires stabilization as a salt compound, often with potassium chloride (KCl) or sodium chloride (NaCl), resulting in a purity level of 74%. In contrast, GH has a purity of 99%. Therefore, a dose of 1500 mg of GH is equivalent to a dose of 2608 mg of GS [21].

3.1.2. Mechanism of action

Exogenously administered glucosamine has pharmacological effects on cartilage and chondrocytes. It impacts osteoarthritis symptoms and pathogenesis by downregulating the expression of various inflammatory and degenerative mediators, thereby reducing cartilage degradation and slowing disease progression. In vitro studies have demonstrated that GS can reduce prostaglandin E2 (PGE2) production and inhibit the activation of the nuclear factor kappa B (NF-κB) pathway, which suppresses the intracellular cytokine signaling cascade in chondrocytes and synovial cells. In osteoarthritis, glucosamine reverses the inflammatory and degenerative effects induced by interleukin-1 (IL-1). IL-1β is a potent inflammatory cytokine produced in high amounts in inflamed joint tissues, where it triggers the expression of inflammatory factors such as cyclooxygenase-2 (COX-2) [9].

A study by Hiba Murtadha Al-Saadi and colleagues from the Faculty of Pharmacy and Faculty of Medicine, Universiti Kebangsaan Malaysia, Cheras, Kuala Lumpur, Malaysia reported that glucosamine supplementation reduced proteoglycan loss, slowed cartilage degeneration, prevented joint space narrowing, and alleviated osteoarthritis pain in both animal models and patients with arthritis. Glucosamine reduced pain, improved joint function and mobility, and decreased cartilage degradation in arthritis patients. Additionally, glucosamine supplementation for 2 years and 6 months reduced the risk of knee osteoarthritis, as evidenced by preventing joint space narrowing on X-rays [10].

3.1.3. Summary of studies on the effectiveness of glucosamine

Table 2: *Some studies on the effectiveness of glucosamine*

No.	Type and dosage of glucosamine used	Research object	Conclusion	Ref.
1	Glucosamin sulfate and Chondroitin sulfate (GS/CS)	Subjects over 40 years of age, diagnosed with knee OA grade 1 to 3 according to the	The new fixed-dose formulation of GS/CS is effective in the treatment	[11]

No.	Type and dosage of glucosamine used	Research object	Conclusion	Ref.
		Kellgren-Lawrence radiographic classification, clinically diagnosed with pain and functional limitation, and a score ≥ 4 cm on the visual analog scale (VAS) (range 0 to 10 cm) were enrolled	of knee osteoarthritis, showing good safety and tolerability	
2	Glucosamin sulfate (GS; 1500 mg) and Chondroitin sulfate cow (CS; 1200 mg)	≥ 40 years old; Diagnosed with knee arthritis	A new formulation of a fixed-dose combination of bovine glucosamine sulfate and chondroitin sulfate was non-inferior to the reference product in the symptomatic treatment of knee osteoarthritis, with a high response rate and good tolerability	[12]
3	Experimental group: 1500/1200 mg Glucosamine HCl/Chondroitin (GH/YES) plus physical therapy Control group: 1500/1200 mg GH/CS	30 patients above 50 years of age with knee osteoarthritis at Islamabad Physiotherapy Clinic and Neurology Council	GH/CS combined with physical therapy is very effective in reducing patient pain, improving function, mobility and quality of life compared to GH/CS alone	[13]
4	Divided into 2 groups: (A) with HPLT+GS 1500mg (GS - Dona®, Rottapharm, Monza, Italy) (n=45) or in control group (B) with HPLT + placebo (n=45).	Characteristics High Power Laser Therapy+Placebo (n = 42) High Power Laser Therapy+Glucosamine (n = 30) Mean \pm SD age (y) 54 \pm 11 56 \pm 9 Mean \pm SD Arthritis duration (y) 14 \pm 11 12 \pm 11 Mean \pm SD Weight (kg) 80 \pm 19 81 \pm 11	High Power Laser Therapy has a beneficial effect in the treatment of knee osteoarthritis, but when combined with Glucosamine Sulfate, thanks to the synergy of the two interventions, long-lasting effects can be achieved up to 6 months after treatment	[14]

Comments: Most studies found were of combination therapy with glucosamine and chondroitin. The studies showed that combination therapy was effective and safe in treating osteoarthritis.

3.2. Chondroitine

3.2.1. Definition

Chondroitin sulfate is composed of large glycosaminoglycans and unbranched saccharide polymers consisting of long chains of d-glucuronic acid monosaccharides and N-acetyl-d-galactosamine. Chondroitin is found in connective tissues, synovial fluid, hyaline cartilage, and bone, where it supports compression resistance. These chains are attached to proteins via hydroxyl groups on the serine amino acids in the protein [22]. Chondroitin is commonly derived from the cartilage of bovine, porcine, chicken, and fish sources through extraction and purification. Natural chondroitin sulfate has a molecular weight (MW) of 50-100 kDa; however, extraction reduces this molecular weight to approximately 10-40 kDa [23].

3.2.2. Mechanism of action

Chondroitin sulfate has anti-inflammatory and immunomodulatory effects, as well as beneficial effects on osteoarthritis. A study by H.-C. Hsu *et al.* found that chondroitin sulfate exerts anti-inflammatory and cartilage-protective effects by increasing the expression of type II collagen and tissue inhibitors of metalloproteinases (TIMP-1 and TIMP-2), while inhibiting the expression and activity of metalloproteinases. Chondroitin sulfate also reduces the phosphorylation of Akt, I κ B kinase (IKK), I κ B, and p65, while stimulating the production of β -catenin, an important protein for cartilage homeostasis [15].

According to a study by X. Li *et al.*, semisynthetic chondroitin sulfate has three main effects on osteoarthritis: reducing synovial inflammation, decreasing cartilage erosion, and preventing bone loss in a dose-dependent manner. Additional research showed that semisynthetic chondroitin sulfate can effectively reduce the production of TNF- α and IL-1 β in activated macrophages via the NF- κ B pathway. It also inhibits RANKL-induced osteoclast differentiation from macrophages, thereby improving synovial inflammation, cartilage erosion, and bone loss through NF- κ B inactivation [16].

In another study conducted by R. Sevimli *et al.* in 2021, experimental osteoarthritis was induced in 40 New Zealand rabbits by cruciate ligament cutting. The results showed statistically significant regeneration of tissue compared to the control group [17].

A study by Z. Ren, Y. Ji, Y. Wang, and L. Dong investigated chondroitin sulfate (CS) derived from the shark species *Scophthalmus maximus* (CS-SM) and found it effective in treating osteoarthritis in both humans and mice. CS-SM appears to inhibit cartilage degradation, reduce chondrocyte apoptosis, and lower levels of interleukin-1, tumor necrosis factor- α , and prostaglandin E2 in synovial fluid. These findings suggest that oral CS-SM is a promising new therapeutic option for osteoarthritis [18].

3.2.3. Summary of studies on the effectiveness of chondroitin

Table 3: Some studies on the effectiveness of chondroitin

No.	Design study	Type and dosage of Chondroitin used	Research object	Conclusion	Ref.
1	Controlled clinical study	Chondroitin sulfate	70 patients with primary and/or post-traumatic unilateral/bilateral knee and/or hip osteoarthritis (Kellgren-Lawrence grades I-II)	Chondroitin sulfate use is associated with a reduction in local pain syndrome and normalization of musculoskeletal system function	[19]
2	Randomized, double-blind study	Chondroitin sulfate	48 obese subjects with moderate knee osteoarthritis (Test group: 24 subjects, taking 600 mg of non-animal chondroitin daily. Control group: 24 subjects, taking placebo)	Non-animal chondroitin supplementation in obese adults with moderate arthritis improved knee inflammation and function in the short term, confirming a previous study	[20]

Comments: Research shows that chondroitin is effective in treating osteoarthritis.

4. Discussion

Glucosamine and chondroitin are two natural compounds commonly used in treating osteoarthritis. Glucosamine primarily stimulates cartilage and synovial fluid production, improving joint function, while chondroitin maintains cartilage moisture and elasticity, reducing joint degeneration. Numerous studies have shown that combining glucosamine and chondroitin is significantly effective in reducing pain and enhancing motor function in osteoarthritis patients. Clinical trials demonstrate that these compounds not only alleviate symptoms but also slow disease progression. Furthermore, glucosamine and chondroitin reduce the need for non-steroidal anti-inflammatory drugs (NSAIDs), thereby minimizing the associated side effects of these medications.

In terms of safety, available data indicate that both glucosamine and chondroitin are safe for long-term use, with side effects being mild and infrequent, such as gastrointestinal disturbances or skin allergies. This safety profile has been confirmed through numerous large-scale studies and meta-analyses, making them a viable choice for osteoarthritis patients. However, the effectiveness of glucosamine and chondroitin remains controversial, and additional research is needed to confirm their optimal dosage and role

in treatment. In summary, glucosamine and chondroitin are not only effective but also safe for osteoarthritis treatment, making them a valuable addition to osteoarthritis management and improving patients' quality of life.

5. Conclusion

This review provides an overview of the mechanisms and data from studies on the effectiveness of glucosamine and chondroitin in treating osteoarthritis. The results indicate that both glucosamine and chondroitin are effective and safe for managing osteoarthritis.

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TÓM TẮT

TỔNG QUAN TÀI LIỆU VỀ GLUCOSAMIN VÀ CHONDROITIN TRONG ĐIỀU TRỊ VIÊM XƯƠNG KHỚP (OSTEOARTHRITIS)

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Ngày nhận bài 21/5/2024, ngày nhận đăng 26/8/2024

Viêm xương khớp (osteoarthritis) là một bệnh lý mạn tính với tổn thương sụn khớp là chủ yếu. Ở Việt Nam, bệnh viêm xương khớp chiếm tỷ lệ cao trong các bệnh lý cơ xương khớp, đặc biệt là ở khớp gối. Gần đây, các thuốc chống thoái hóa khớp có tác dụng chậm, bao gồm glucosamin, chondroitin sulfat, diacerein... đã được đề xuất như một phương pháp điều trị dược lý quan trọng. Tuy nhiên, tài liệu bằng tiếng Việt về các hoạt chất này còn hạn chế. Vì vậy, chúng tôi thực hiện bài báo này nhằm tổng quan tài liệu về hiệu quả và an toàn của các thuốc này, từ đó nâng cao hiệu quả sử dụng nhóm thuốc này trên lâm sàng. Kết quả cho thấy glucosamin và chondroitin có hiệu quả và an toàn trong điều trị viêm xương khớp từ các dữ liệu đã được tìm kiếm và phân tích trong bài báo.

Từ khóa: Glucosamin; chondroitin; viêm xương khớp.