

Evaluation of the Effectiveness of a Kind of Nutritious Supplement on Pain and Joint Function in Patients with Knee Osteoarthritis

Abstract

Introduction: Osteoarthritis (OA) is a common joint problem that primarily affects the knee joint, leading to significant disability and imposing a substantial burden on healthcare systems. Therefore, treatment aimed at minimizing physical dysfunction in these patients is of great importance. This study aimed to assess how well a type of nutritional supplement works to reduce pain and improve joint function in people with knee osteoarthritis.

Materials & Methods: This study was a randomized, double-blind clinical trial conducted on patients who presented to the orthopedic clinics in one year. Patients in the intervention group received a kind of nutritious supplement along with standard therapy, but control group received standard therapy with a placebo. Statistical analyses were performed using SPSS version 20, with the significance level described 0.05.

Results & Discussion: The mean age was 58.93 ± 5.65 years in the control and 59.77 ± 6.44 years in intervention groups, and no statistically significant difference between them ($P > 0.05$). Results from multiple covariance regression analysis demonstrated a statistically significant difference between the two groups in terms of pain severity, symptom scores, functional capacity, and total WOMAC score ($P < 0.05$).

Conclusion: Daily administration of this nutritious supplement for up to two months, in addition to standard therapy, is recommended for patients with knee osteoarthritis. This regimen can result in clinically meaningful improvement in pain, symptom severity, functional capacity, and total WOMAC score.

Keywords: Food assistance, Osteoarthritis, Knee, Functional status, Pain.

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Introduction

Osteoarthritis (OA) is one of the most prevalent joint disorders, particularly affecting the knee joint. This condition results in progressive degeneration and thinning of articular cartilage, bone-on-bone friction, and increased inflammation in the synovial fluid. These processes lead to clinical manifestations such as joint swelling, pain, reduced range of motion, stiffness, and joint instability⁽¹⁾. Contributing factors for knee osteoarthritis include trauma, excessive load due to obesity, strenuous physical activities such as mountaineering and football, genetic predisposition, as well as septic and aseptic arthritis. The prevalence of osteoarthritis rises with age. Although it is more commonly observed among the elderly, degenerative and inflammatory changes of the joints can occur in adults of all ages, particularly athletes. Osteoarthritis of knee is a common reason of disability, especially functional impairment, and imposes considerable costs on patients and healthcare systems⁽²⁾. It is estimated that, with an aging population in the United States, the prevalence of osteoarthritis will increase by 10–66% by 2024, thereby greatly escalating its economic burden⁽³⁾. Symptomatic knee OA occurs in approximately 12% of individuals over 60 years of age and 6% of all adults over 30 years of age in the United States⁽⁴⁾.

The primary therapeutic goals in knee OA include pain relief and preservation of physical function. Compounds that stimulate cartilage synthesis, inhibit cartilage degradation, and reduce intra-articular inflammation may play a key role in slowing disease progression, alleviating symptoms, and reducing the required dosage of conventional drugs.

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Current pharmacological treatments cover a wide spectrum, and surgical interventions are reserved for advanced cases^(5,6). However, due to the limited efficacy of available medications, research into novel treatment approaches remains an area of interest.

Simotriax tablets are supplied in packs of 60. Each tablet contains glucosamine hydrochloride, chondroitin sulfate, methylsulfonylmethane (MSM), vitamin D3, as well as excipients such as povidone, magnesium stearate, and croscarmellose sodium⁽⁷⁾.

Chondroitin sulfate and glucosamine sulfate produces useful results on the metabolism of joint-derived cells in experimental models, including chondrocytes, synoviocytes, and subchondral bone cells, each play critical roles in pathogenesis of osteoarthritis. These compounds enhance type II collagen and proteoglycan synthesis in articular chondrocytes of human, Stop the making of substances that cause inflammation and break down proteins, lower cell death, and help balance the build-up and breakdown of the cartilage outside the cells (ECM). Clinical trials have shown favorable effects of chondroitin sulfate and glucosamine on pain and functional outcomes, with recent meta-analyses showing modest but significant reductions in joint space narrowing. Accordingly, international guidelines recommend these agents for treatment of osteoarthritis in hip and knee joints⁽⁸⁾.

Methylsulfonylmethane (MSM), a naturally occurring organosulfur compound found in different types of plants, has demonstrated several biological features, including anti-inflammatory and antioxidant effects, in both laboratory and clinical studies. MSM has been widely used as a dietary supplement for its analgesic, anti-inflammatory, and antioxidant benefits⁽⁹⁾.

Vitamin D supplementation has been shown to significantly reduce OA-related pain, inflammation, cartilage degradation, and levels of matrix metalloproteinases (MMPs). In addition, vitamin D decrease the pro-inflammatory cytokines such as TNF- α , IL-1 β , and IL-6⁽¹⁰⁾. Vitamin D2 supplementation may decrease oxidative protein damage, alleviate pain (VAS scores), improving the quality of life, grip strength, and physical function in osteoarthritis of joints⁽¹¹⁾.

Available evidence suggests that the kind of nutritious supplement, due to its multi-component formulation, may reduce joint stiffness and swelling, enhance mobility and flexibility, support cartilage repair and regeneration, and increase synovial fluid concentration⁽⁷⁾. Nevertheless, further clinical

evidence is required. This study was made to see how well a special healthy supplement helps decrease pain and joint function improvement in patients with osteoarthritis of knee.

Materials & Methods

This study was set up as a randomized, double-blind clinical trial and was carried out on patients who attended orthopedic clinics affiliated with Mazandaran University of Medical Sciences in 2024. Patients were randomly dedicated to either the intervention or control group using block randomization.

Inclusion criteria: (1) patients aged 50–70 years diagnosed with knee osteoarthritis confirmed by a specialist and graded as 2 or 3 on radiographs; (2) absence of diabetes mellitus and hypertension; and (3) providing written informed consent to participate in the study.

Exclusion criteria: (1) a history of systemic diseases, (2) a history of infectious diseases, (3) a history of vascular disorders, (4) coagulation abnormalities, and (5) severe knee deformities or structural abnormalities.

Intervention group (the kind of nutritious supplement): Participants in this group received the kind of nutritious supplement in addition to standard therapy, which consisted of diclofenac sodium (administered according to the recommended dosing regimen), physiotherapy, and joint warming.

Control group (placebo): Participants in this group received the same standard therapy as above (diclofenac sodium, physiotherapy, and joint warming) along with a placebo. The placebo tablets were identical in appearance and packaging to the kind of nutritious supplement and were manufactured by the same company producing the active drug.

Outcome measures and assessment

Joint function was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which assess pain, stiffness, and physical function.

Baseline assessment: Before the intervention, baseline evaluations were performed for each participant. These included collection of demographic data, pain assessments, and functional joint tests.

Post-intervention assessment: After 30 to 60 days, participants were re-evaluated. Pain questionnaires and joint function tests were completed and recorded at follow-up.

Statistical Analysis

Quantitative variables were summarized using measures of central tendency and dispersion (mean \pm standard deviation), and qualitative variables were presented as frequencies (percentages). Prior to statistical analyses, We checked if the quantitative variables followed a normal distribution using the Kolmogorov–Smirnov test. To compare the average numbers between the group that received the treatment and the group that did not, the independent samples t-test was applied when data followed a normal distribution; otherwise, the non-parametric Mann–Whitney U test was used. To compare the distribution of qualitative variables between groups, the chi-square test or Fisher’s exact test was employed, as appropriate.

In addition, to compare WOMAC subscale scores and the total WOMAC score between the two groups while controlling for potential confounders such as age, sex, and baseline scores, a multiple covariance regression analysis (ANCOVA) model was applied. All statistical analyses were conducted using SPSS version 20, with a significance level set at 0.05.

Results

64 patients were enrolled in this study and were randomly assigned into two groups of 32 patients each (intervention and control group). In the intervention group, five patients discontinued the study due to adverse effects, leaving 27 patients who completed the treatment protocol. In the control group, 18 patients (56.20%) were female and 14 (43.80%) were male, while in the intervention group, 14 patients (51.90%) were female and the remaining participants were male. Chi-square test results showed no statistically significant difference in sex distribution between the two groups ($P = 0.73$) (Figure 1). The mean age of participants in the control group was 58.93 ± 5.65 years, compared with 59.77 ± 6.44 years in the intervention group. According to the Mann–Whitney U test, there was no important difference in average age between the two groups ($P = 0.40$) (Figure 2). Therefore, the control

and intervention groups were comparable in terms of age and sex.

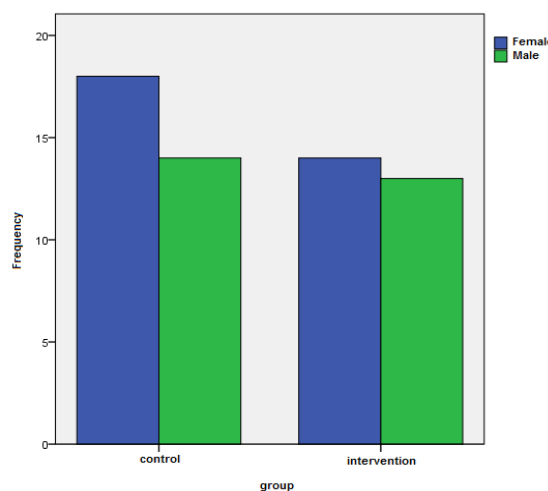


Figure 1: Distribution of sex in the control and intervention groups.

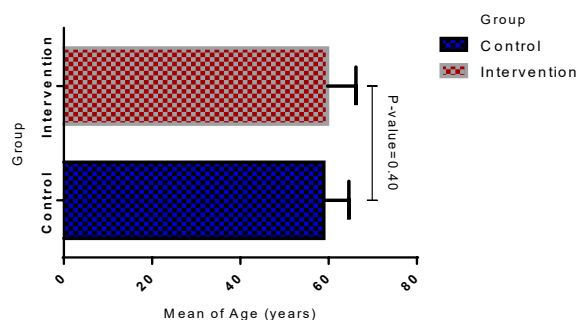


Figure 2: Comparison of mean age between the control and intervention groups.

Comparison of WOMAC Subscale Scores and Total Score Between two Groups Over Time

Based on patient responses to the 33 items of the WOMAC questionnaire, subscale and total scores were converted to a 0–100 scale, and higher scores indicated better outcomes and greater improvement. The WOMAC results are presented in Table 1.

At the start, the Mann–Whitney U test showed a meaningful difference between the two groups only in the stiffness measurement ($P < 0.05$). No significant differences were observed in the mean scores of the other subscales or in the total WOMAC score between the two groups ($P > 0.05$). At post-intervention assessment, Mann–Whitney U test. The results showed differences between the control group and the group that received the intervention in

all the WOMAC subscales and the total score ($P < 0.05$). To evaluate within-group changes over time, for comparing the mean WOMAC subscale and total scores in the intervention group, the Wilcoxon signed-rank test was used. In the control group, statistically significant differences were seen in each subscales and the total score between baseline and post-intervention ($P < 0.05$).

Similarly, in the intervention group, statistically significant improvements were observed in each subscales and the total WOMAC score over time ($P < 0.05$), indicating that the intervention effect was statistically significant.

Comparison of WOMAC Outcomes Between Two Groups After Adjustment for Confounders

To compare WOMAC subscale and total scores between the two groups while controlling for confounding variables (age, sex, and baseline scores), a multiple covariance regression analysis (ANCOVA)

model was applied. The results of the ANCOVA analyses are presented in Tables 2–6.

After adjustment for the effects of age, sex, and baseline symptom scores, a statistically significant difference was found in symptom severity between two groups ($P < 0.05$).

Specifically, the mean symptom subscale score in the intervention group was, on average, 15.30 units greater than in the control group. This finding indicates that the intervention produced a significant effect in reducing patients' symptom severity ($P < 0.05$) (Table 2).

Comparison of WOMAC Outcomes Between the Control and Intervention Groups After Adjustment for Confounders (continued)

After adjustment for the confounding effects of age, sex, and baseline stiffness, no statistically significant difference in stiffness scores was seen between the two groups ($P > 0.05$).

Table 1: Comparison of Mean WOMAC Questionnaire Scores (out of 100) Between Control and Intervention Groups Over Time

Subscale	Timepoint	Group		Test result
		Control	Post-intervention	
Symptoms	Baseline	9.35±50.00	10.33±65.33	0.85
	Post-intervention	8.45±03.00	10.59±31.44	< 0.001*
Result		< 0.001*	< 0.001*	
Stiffness	Baseline	13.40±83.62	3.26±55.24	< 0.001*
	Post-intervention	8.50±98.00	10.58±86.79	0.004*
Result		0.024*	< 0.001*	
Pain	Baseline	6.45±46.83	4.45±04.16	0.75
	Post-intervention	7.51±05.38	7.67±39.79	< 0.001*
Result		0.013*	< 0.001*	
Function (ADL)	Baseline	6.54±79.04	4.56±30.59	0.32
	Post-intervention	11.59±10.55	9.74±39.40	< 0.001*
Result		< 0.001*	< 0.001*	
Total WOMAC	Baseline	2.48±07.10	3.48±80.03	0.45
	Post-intervention	7.54±13.54	7.69±33.68	< 0.001*
Result		< 0.001*	< 0.001*	

* Significant at the 0.05 level. Values are reported as Mean ± Standard Deviation.

Table 2: Comparison of Symptom Severity Between two Groups Using Multiple Covariance Regression Model with Adjustment for Confounders

Variable (Reference Level)	Coefficient (95% Confidence Interval)	P-value
Group (Control)	-	< 0.001*
Intervention	15.30 (19.41,11.18)	

* Significant at the 0.05 level. Adjusted for age, gender, and baseline symptom measurement.

Although the mean stiffness subscale score in the intervention group was on average 4.85 units higher than in the control group, this difference was not statistically significant, indicating that the intervention did not have a meaningful effect on reducing stiffness ($P > 0.05$) (Table 3).

After adjusting for the confounding effects of age, sex, and baseline pain, a statistically significant difference in pain scores was observed between the two groups ($P < 0.05$). The mean pain subscale score in the intervention group was, on average, 16.11 units higher than in the control group, indicating that the intervention had a significant effect in improving patients' pain ($P < 0.05$) (Table 4).

After taking into account the effects of age, gender, and starting abilities, a significant difference in

performance scores was found between the intervention and control groups ($P < 0.05$).

The mean function subscale score in the intervention group was, on average, 11.19 units higher than in the control group, suggesting that the intervention significantly improved patients' functional outcomes ($P < 0.05$) (Table 5). After considering the effects of age, sex, and initial WOMAC scores, we found a significant difference in total WOMAC scores between the intervention and control groups ($P < 0.05$). The mean total WOMAC score in the intervention group was, on average, 14.68 units higher than in the control group. This indicates that, overall, the intervention had a statistically significant positive effect on patients' condition as measured by the WOMAC questionnaire ($P < 0.05$) (Table 6).

Table 3: Comparison of stiffness between the two groups using multiple covariance regression analysis adjusted for confounders

Variable (Reference Level)	Coefficient (95% CI)	P-value
Control Group	–	0.130
Intervention	4.85 (–1.58, 11.29)	–

Significant at the 0.05 level. # Adjusted for age, sex, and baseline stiffness.

Table 4: Comparison of pain between the control and intervention groups using multiple covariance regression analysis adjusted for confounders

Variable (Reference Level)	Coefficient (95% CI)	P-value
Control Group	–	<0.001
Intervention	16.11 (12.47, 19.76)	–

Significant at the 0.05 level. # Adjusted for age, sex, and baseline pain.

Table 5: Comparison of function between the control and intervention groups using multiple covariance regression analysis adjusted for confounders

Variable (Reference Level)	Coefficient (95% CI)	P-value
Control Group	–	<0.001
Intervention	11.19 (7.53, 14.84)	–

Significant at the 0.05 level. # Adjusted for age, sex, and baseline function.

Table 6: Comparison of WOMAC total score between the control and intervention groups using multiple covariance regression analysis adjusted for confounders

Variable (Reference Level)	Coefficient (95% CI)	P-value
Control Group	–	<0.001
Intervention	14.68 (11.22, 18.13)	–

Significant at the 0.05 level. # Adjusted for age, sex, and baseline WOMAC total score.

Discussion

The present study demonstrated that adjunctive administration of the kind of nutritious supplement in osteoarthritis of knee over a 30–60 day period led to significant improvements in the WOMAC subscales of pain, symptoms, physical function, and total score compared with placebo. These differences remained robust even after adjustment for potential confounding factors including age, sex, and baseline values. Only in the stiffness subscale, despite an increase in the mean score in the intervention group, no statistically significant difference was observed after adjustment. This pattern suggests that the active components of the kind of nutritious supplement primarily exert their effects through reducing inflammation and pain and enhancing cartilage matrix repair, while mechanisms underlying the perception of stiffness may require longer intervention durations or may be more dependent on disease burden.

Our findings are compatible with prior documents about the beneficial effects of the key constituents of the present formulation. The efficacy of glucosamine and chondroitin in improving pain and function as well as slowing joint space narrowing has been documented in recent meta-analyses. These agents stimulate type II collagen and proteoglycan synthesis and inhibit metalloproteinase production, thereby shifting the cartilage anabolic–catabolic balance toward repair. Methylsulfonylmethane (MSM), with its anti-inflammatory and antioxidant properties, can suppress NF- κ B signaling and pro-inflammatory cytokine production, thus reducing cartilage degradation⁽⁹⁾. Vitamin D supplementation has also been shown in both animal and human studies to reduce pain, prevent cartilage breakdown, and inhibit expression of MMPs, TNF- α , and IL-6⁽¹⁰⁾; clinical trials have reported that adequate dosing of vitamin D reduces VAS pain and improves strength and quality of life in OA patients⁽¹¹⁾. The synergistic action of these components in a single preparation may therefore produce cumulative effects on inflammatory and reparative pathways, as supported by our findings.

It is noteworthy that improvements were also observed in the control group, likely attributable to standard treatments (diclofenac, physiotherapy, heat therapy) and educational support. However, the effect size in the intervention group was significantly greater. Multivariate ANCOVA demonstrated that the

adjusted mean differences in pain and function scores were 16.11 and 11.19 units, respectively, in favor of the kind of nutritious supplement. Considering that the minimal clinically important difference (MCID) for pain and function on the 100-point WOMAC scale has been reported to be approximately 10–12 units⁽⁵⁾, these results indicate that the observed improvements are not only statistically but also clinically meaningful.

With regard to stiffness, the absence of a significant difference may be explained by two factors: first, the reduced effective sample size after patient dropout ($n = 27$), which limited statistical power to detect small changes; second, the possibility that longer treatment duration is required to improve stiffness arising from structural alterations in the capsule and synovium. Studies with follow-up beyond three months have demonstrated that chondroprotective compounds exert more pronounced delayed effects on stiffness⁽⁸⁾; thus, future trials should be designed with longer follow-up intervals.

Comparison with previous studies on individual components is also important. In a systematic review, Henrotin et al. reported that chondroitin sulfate reduced WOMAC pain by an average of 11 units⁽⁸⁾. The present study showed greater pain relief, which may be attributable to the combined effect of MSM and vitamin D. Furthermore, in a meta-analysis by Meng et al. on biologic agents for OA, mean pain reduction was approximately 8 units and functional improvement about 6 units⁽⁹⁾. Therefore, the kind of nutritious supplement provides comparable or even superior effects within a relatively short timeframe, and from a cost-effectiveness perspective, may hold particular value in national treatment protocols.

From a mechanistic standpoint, the components of the kind of nutritious supplement are likely to target multiple pathways: inhibition of inflammatory cyclooxygenases, reduction of free radicals, induction of matrix protein synthesis, and modulation of nitric oxide synthase. This multi-target approach aligns with the multifactorial pathogenesis of osteoarthritis⁽³⁾ and may explain why the total WOMAC score improved by 14.68 units.

Despite the strengths of the study—including randomized double-blind design, use of a matched placebo, and control of confounders—several limitations should be accepted: (1) the single-center nature of the trial and recruitment from a university clinic in Mazandaran, which may limit generalizability; (2) relatively short follow-up and

absence of imaging assessments (MRI or serial radiographs) to confirm structural changes; (3) dropout of five patients in the intervention group, which, although addressed by intention-to-treat analyses, may have reduced statistical power; and (4) lack of measurement of serum inflammatory markers or cartilage biomarkers, which could have strengthened clinical–laboratory correlations. Future multicenter studies with larger sample sizes, at least six months of follow-up, and inclusion of biochemical indices are recommended to better establish the durability and long-term safety of the drug.

Regarding safety, no serious adverse events were reported in the intervention group, and the dropout of five participants was due to mild side effects. This finding is consistent with the favorable safety profiles of the drug's components reported in previous studies^(8,9). Nevertheless, caution is advised regarding potential interactions of glucosamine with anticoagulants and monitoring of renal function during long-term MSM use

Conclusion

Daily administration of the kind of nutritious supplement for up to two months, in addition to standard therapy, can provide clinically remarkable improvements in pain, symptoms, physical function, and total WOMAC score in patients with osteoarthritis of knee, showing a clear superiority over placebo. Given its lower cost compared with biologic agents and ease of administration, the kind of nutritious supplement may serve as a valuable adjunct in the first-line management of OA. Longer-term trials with direct comparisons against other common supplements are warranted to consolidate the evidence base.

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References

- 1 Kan H, Chan P, Chiu K, Yan C, Yeung S, Ng Y, et al. Non-surgical treatment of knee osteoarthritis. *Hong Kong Med J*. 2019;25(2):127-133. DOI: 10.12809/hkmj187600.
- 2 Whitaker K.M, Gabriel K.P, Laddu D, White D.K, Sidney S, Sternfeld B, et al. Bidirectional associations of accelerometer measured sedentary behavior and physical activity with knee pain, stiffness, and physical function: The CARDIA study. *Prev Med Rep*. 2021;22:101348. DOI: 10.1016/j.pmedr.2021.101348.
- 3 Mora JC, Przkora R, Cruz-Almeida Y. Knee osteoarthritis: pathophysiology and current treatment modalities. *J Pain Res*. 2018;11:2189. DOI: 10.2147/JPR.S154002.
- 4 Hsu H, Siwiec R.M. Knee osteoarthritis. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. 2023 Jun 26. Bookshelf ID: NBK507884
- 5 Dantas L.O, de Fátima Salvini T, McAlindon T.E. Knee osteoarthritis: key treatments and implications for physical therapy. *Braz J Phys Ther*. 2021;25(2):135-46. DOI: 10.1016/j.bjpt.2020.08.004.
- 6 Katz J.N, Arant KR., Loeser R.F. Diagnosis and treatment of hip and knee osteoarthritis: a review. *JAMA*. 2021;325(6):568-78. DOI: 10.1001/jama.2020.22171.
- 7 Simorgh Darou Attar Company. SIMO TRIFLEX. <https://simorghdarou.com/en/product/simo-triflex-en/> [cited 2025 Oct 26]
- 8 Henrotin Y, Marty M, Mobasheri A. What is the current status of chondroitin sulfate and glucosamine for the treatment of knee osteoarthritis? *Maturitas*. 2014;78(3):184-7. DOI: 10.1016/j.maturitas.2014.04.015.
- 9 Meng F, Li H, Feng H, Long H, Yang Z, Li J, et al. Efficacy and safety of biologic agents for the treatment of osteoarthritis: a meta-analysis of randomized placebo-controlled trials. *Ther Adv Musculoskelet Dis*. 2022;14:1759720x221080377. DOI: 10.1177/1759720x221080377.
- 10 Hsiao A.F, Lien Y.C, Tzeng I.S, Liu C.T, Chou S.H, Horng Y.S. The efficacy of high- and low-dose curcumin in knee osteoarthritis: A systematic review and meta-analysis. *Complement Ther Med*. 2021;63:102775. DOI: 10.1016/j.ctim.2021.102775.
- 11 Yang L, Wu BY, Ma L, Li ZD, Xiong H. Comparative efficacy and safety of Chinese herbal medicine for knee osteoarthritis: A protocol for systematic review and network meta-analysis. *Medicine (Baltimore)*. 2021;100(29):e26671. DOI: 10.1097/MD.00000000000026671.