J Med Biosci Suppl 2026:8: S35 - S44 DOI: 10.58837/CHULA.JMBS.8.suppl.5

Original article

Curcumin supplementation lowers serum IL-1β and IL-6 levels and increases physical functions in knee osteoarthritis patients

Kongpob Wanikanukul[1], Sitthinee Leena[2], Suphattra Phakham[3], Suvichada Assawakosri[4], Sittisak Honsawek[1,*]

[1]Center of Excellence in Osteoarthritis and Musculoskeleton, Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand
[2]Biomedical Science, Faculty of Science, Mahidol University, Bangkok, Thailand
[3]Public Health Program, Faculty of Health Sciences, Siam Technology College, Bangkok, Thailand
[4]Department of pharmacology, Faculty of Science, Mahidol University, Bangkok, Thailand

Abstract

Background: Knee osteoarthritis (KOA) is a degenerative joint disease driven by low-grade chronic inflammation. Long-term dependence on non-steroidal anti-inflammatory drugs (NSAIDs) is constrained by serious systemic risks, highlighting the clinical need for safe, bioavailable adjuvant therapies such as curcumin phytosome.

Objectives: This study aimed to evaluate the efficacy of daily curcumin phytosome supplementation versus placebo in primary KOA, with oral naproxen restricted to as-needed (PRN) rescue analgesia.

Methods: In this 4-week randomized, single-blind, parallel-group trial, 74 patients with primary KOA (Kellgren–Lawrence grades 1–2) received either curcumin phytosome (250 mg twice daily; n = 52) or matching placebo (n = 22). Oral naproxen (250 mg) was permitted only as rescue medication. Serum interleukin (IL)-1β and IL-6 levels, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Visual Analogue Scale (VAS), and physical performance tests, including the 3-minute walk test (3-MWT), gait speed test (GST), chair stand test (CST), and timed up and go (TUG) test, were assessed at baseline and week 4. Changes from baseline (Δ) were compared between groups using the Mann–Whitney U test.

Results: Compared with the placebo group, curcumin supplementation demonstrated significantly greater reductions in serum IL-1β ($P = 0.001$) and IL-6 ($P = 0.0282$). Significant improvements were also observed in WOMAC pain ($P = 0.0038$), stiffness ($P = 0.0043$), physical function ($P < 0.0001$), total WOMAC score ($P < 0.0001$), VAS pain score ($P < 0.05$), GST ($P = 0.039$), and TUG ($P = 0.0174$). There were no significant differences in the 3-MWT and CST between placebo group and curcumin group.

Conclusions: Daily curcumin supplementation resulted in greater reductions in serum IL-1β and IL-6 as well as greater improvements in pain, physical function, and selected mobility outcomes, compared with placebo in primary KOA patients.

Keywords: curcumin, knee osteoarthritis (KOA), interleukin-1 beta (IL-1β), interleukin-6 (IL-6), WOMAC, physical functions

***Correspondence to:** Kongpob Wanikanukul, Center of Excellence in Osteoarthritis and Musculoskeleton, Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand
E-mail: kongpob7709@gmail.com
Received: 4 May 2026
Revised: 22 June 2026
Accepted: 26 June 2026

Open Access 2026 Wanikanukul et al ., published by Faculty of Medicine, Chulalongkorn University. This work is licensed under the Creative Commons Attribution 4.0 International License.

Knee osteoarthritis (KOA) is the most prevalent progressive articular disorder among older adults, acting as a primary contributor to locomotor disability, functional dependence, and socioeconomic burden worldwide. [1] Epidemiological data from the global burden of disease study indicate that KOA affects over 595 million people worldwide, representing a 132.0% increase in absolute prevalence over the past three decades. [1] This rapid increase is driven by population aging alongside the global obesity epidemic, both of which accelerate cumulative mechanical loading across the weight-bearing surfaces of the knee. [1, 2] In Thailand, KOA imposes a substantial burden on public health system, with a high prevalence among postmenopausal women and individuals over 60 years of age, resulting in substantial clinical morbidity and impaired quality of life. [3-5]

Historically, KOA was regarded as a passive, mechanical disorder characterized by the degeneration of articular cartilage. However, recent biomedical evidence indicates that KOA is a heterogeneous, whole-joint disease mainly driven by persistent, low-grade chronic inflammation. [6] The molecular pathology involves multiple joint tissues and results in progressive articular cartilage degradation, subchondral bone remodeling, osteophyte formation at joint margins, and chronic synovial membrane inflammation (synovitis). [1, 6] This degenerative process is mediated by networks of pro-inflammatory cytokines, with interleukin (IL)-1 beta and IL-6 acting as key upstream molecular regulators. These cytokines activate intracellular signaling pathways in articular chondrocytes, particularly the nuclear factor-kappa B (NF-κB) and mitogen-activated protein kinase (MAPK) cascades. [7] Activation of these pathways induces a catabolic cellular phenotype, indicated by increased production of matrix metalloproteinases (such as MMP-13) and disintegrins and metalloproteinases with thrombospondin motifs (such as ADAMTS-4 and ADAMTS-5). These proteolytic enzymes degrade type II collagen and aggrecan, leading to irreversible extracellular matrix (ECM) degradation. Elevated circulating IL-6 levels are closely associated with the clinical severity of joint pain, stiffness, and structural progression. [7, 8]

Standard drug treatment of KOA relies heavily on oral non-steroidal anti-inflammatory drugs (NSAIDs) for pain management through cyclooxygenase (COX) inhibition. However, continuous NSAID administration carries well-documented risks, including upper gastrointestinal mucosal ulceration and bleeding, renal impairment, and adverse cardiovascular events. [9] These complications are particularly concerning for elderly patients presenting with multiple comorbidities, emphasizing the distinct clinical demand for safe, targeted anti-inflammatory regimens. [10]

Curcumin, a natural lipophilic polyphenol extracted from the rhizome of turmeric (*Curcuma longa* L.), exhibits broad anti-inflammatory effects by inhibiting IκB kinase (IKK) phosphorylation and subsequent NF-κB nuclear translocation, which down-regulates the transcription of IL-1β and IL-6. Although curcumin demonstrates therapeutic promise, its clinical application is limited by poor aqueous solubility, rapid intestinal metabolism, and low systemic bioavailability. To overcome these pharmacokinetic limitations, delivery systems such as curcumin phytosome, which complexes curcumin with dietary phospholipids, have been developed to enhance gastrointestinal absorption and peripheral tissue distribution. [11-17]

Although previous studies have shown that curcumin improves patient-reported clinical indices, such as Visual Analogue Scale (VAS) and Western Ontario and McMaster Universities Arthritis Index (WOMAC) [3-5, 18, 19], there is a lack of trials that validate these subjective outcomes using timed, objective physical performance tests and concurrent measurements of circulatory cytokine modulation. The objective of this study was to evaluate the effects of curcumin phytosome on serum inflammatory cytokines (IL-1β and IL-6) and physical functions in KOA patients.

Materials and methods

Study design

This study was designed as a 4-week, prospective, randomized, single-blind, parallel-group clinical trial conducted at the outpatient department of Orthopaedic Surgery, King Chulalongkorn Memorial Hospital, Bangkok, Thailand. Participants were blinded to treatment allocation throughout the study, whereas investigators responsible for dispensing the interventions were aware of group assignments. The trial assessed the efficacy of daily curcumin phytosome compared to placebo, with both groups permitted to use an oral NSAID as needed for rescue therapy.

The present study was approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University (COA no. 1018/2025). Written informed consent was obtained from all participants prior to enrollment. The study was registered with the Thai Clinical Trials Registry (TCTR; Registration No. TCTR20250713002).

Participants and sample selection

Individuals aged 50 to 80 years with symptomatic primary KOA were screened for eligibility. Patients were eligible for inclusion if they had radiographic confirmation of Kellgren-Lawrence grade 1–2. Conversely, patients were systematically excluded if they presented with secondary or inflammatory arthropathies (such as rheumatoid arthritis or gout), active septic arthritis, a history of knee surgery, significant joint trauma, musculoskeletal tumors or immunodeficiencies. The required sample size was determined using G*Power software (version 3.1.9.7). Assuming a two-tailed alpha level (α) of 0.05, a statistical power ($1-\beta$) of 0.80, and a moderate-to-large expected effect size (d = 0.65) based on serum cytokine variances reported in closely related literature. [20] Ultimately, 74 participants completed all study phases and were included in the final analysis: 22 in the placebo group and 52 in the curcumin (CUR) group.

Interventions and clinical monitoring

Seventy-four participants were allocated into two parallel groups based on a consecutive entry sequence. The curcumin group (n = 52) received curcumin phytosome (CURCARE® PHYTO, 250 mg per capsule, formulated with phospholipids for enhanced bioavailability) twice daily after breakfast and dinner, totaling 500 mg per day for 4 weeks. The control group (n = 22) received placebo capsules in appearance and weight, administered on the same schedule.

Both groups were instructed to avoid daily use of NSAIDs. Naproxen 250 mg tablets were provided only as rescue medication for severe joint pain. Participants recorded all rescue medication use in a compliance diary during the 4-week study.

Enzyme-linked immunosorbent assay (ELISA) for IL−1β and IL-6

Venous blood samples were collected from participants at baseline and at week 4 using serum collection tubes. The samples were centrifuged at 4,000 rpm for 10 minutes at 25°C to isolate serum, which was then transferred into microcentrifuge tubes and stored at −80°C until analysis. Serum IL-1β and IL-6 levels were measured using commercial human-specific ELISA kits (ELK Biotechnology, Wuhan, China) following the manufacturer's instructions. Briefly, 100 µL of samples or standards were incubated in pre-coated plates, followed by sequential incubations with 1× biotinylated antibody and 1× streptavidin-horseradish peroxidase. Color development was initiated using 3,3',5,5'-tetramethylbenzidine substrate, and the reaction was quenched with stop reagent. The absorbance was measured immediately using a microplate reader at 450 nm, and cytokine concentrations were calculated based on the respective standard curves.

Clinical scores (VAS and WOMAC)

Patients with KOA were evaluated through face-to-face interviews using standardized questionnaires. These included the VAS, a 10-centimeter horizontal line ranging from 0 (no pain) to 10 (the worst imaginable pain) used to assess subjective pain intensity, and the WOMAC index was a 22-item instrument graded on a 0–10 scale per item that evaluates three health domains: pain (5 items; score range 0–50), stiffness (2 items; score range 0–20), and physical functions (15 items; score range 0–150). Higher total scores indicate worse clinical status.

Physical performance metrics

Objective mobility and physical capability were evaluated using four validated clinical measures, which were combined into a single functional testing protocol. The 3-minute walk test (3-MWT) measured the maximum distance, in meters, that participants could walk along a flat course within three minutes. The gait speed test (GST) evaluated comfortable walking speed over a 4-meters walkway by timing the traversal of the central 4 meters, thereby excluding acceleration and deceleration phases. The faster of two trials determined gait velocity (m/s), which was compared to a clinical threshold of 0.8 m/s. Lower-limb muscular endurance was assessed using the chair stand test (CST), which recorded the time to complete five consecutive sit-to-stand repetitions from a standard 45-cm chair without arm support, with a target time of 12 seconds or less. The timed up and go (TUG) test assessed dynamic balance and mobility by timing participants as they rose from an armchair, walked 3 meters, turned 180 degrees, returned, and sat down, with a clinical threshold of 10 seconds or less.

Table 1. Baseline demographic and clinical characteristics of patients with KOA

Characteristics	Curcumin group (Curcumin + PRN Naproxen) (n=52)	Control group (Placebo + PRN Naproxen) (n=22)	*P*-value
Age (years)	67.62 ±1.02	64.36±1.73	0.1266
Gender; n (%)			
Females	49 (94.23)	17 (77.28)	–
males	3 (5.77)	5 (22.72)	–
Weight (kg)	61.91 ± 1.73	60.47±1.86	0.8487
Height (cm)	155.1 ± 0 1.21	157.30 ± 1.72	0.2074
BMI (kg/m²)	25.83 ± 0.60	24.61 ± 0.75	0.313
IL-1β level (pg/mL)	533.00 ± 44.70	641.1 ± 91.31	0.6091
IL-6 level (pg/mL)	79.80 ± 10.17	49.79 ± 9.38	0.0969
WOMAC (score)			
Pain	18.98 ± 1.22	14.27±1.69	0.0302
Stiffness	7.46 ± 0.54	4.77 ± 0.78	0.0073
Function	53.96 ± 3.01	37.77 ± 5.30	0.0014
Total	80.40 ± 4.26	56.82 ± 6.70	0.0015
VAS (score)	4.50 ± 0.24	3.77 ± 0.50	0.0665
Physical performances			
3MWT (m)	170.30 ± 4.45	182.6 ± 8.62	0.1875
GST (m/s)	0.86 ± 0.03	1.00 ± 0.07	0.032
CST (s)	14.61 ± 0.67	13.04 ± 0.89	0.030
TUG (s)	10.79 ± 0.44	9.07 ± 0.57	0.0007

Data are presented as mean ± standard error of the mean (SEM) or number (%). Baseline comparisons between groups were performed using the Mann–Whitney *U* test for continuous variables and the Chi-square test (or Fisher's exact test, as appropriate) for categorical variables. Statistical significance was defined as $P < 0.05$.

Statistical analysis

Statistical analyses were performed using GraphPad Prism (version 10.2.3, GraphPad software, San Diego, CA, USA). Data normality was assessed using the Shapiro–Wilk test. Continuous variables are presented as mean ± standard error of the mean (SEM), and categorical variables are presented as number (%). Continuous variables are presented as mean ± SEM to facilitate comparison with previous clinical studies, whereas non-parametric tests were used because several variables were not normally distributed. Baseline comparisons between groups were performed using the Mann–Whitney *U* test for continuous variables and the Chi-square test (or Fisher's exact test, as appropriate) for categorical variables. Within-group comparisons between baseline (V1) and week 4 (V2) were performed using the Wilcoxon matched-pairs signed-rank test. To evaluate treatment effects, changes from baseline ($\Delta = V2 - V1$) were calculated for all outcomes and compared between the curcumin and placebo groups using the Mann–Whitney *U* test. A two-sided *P*-value <0.05 was considered statistically significant.

Results

Baseline demographic and clinical characteristics are summarized in **Table 1**. The two groups were comparable in age, sex distribution, body weight, height, body mass index (BMI), serum IL-1β, serum IL-6, VAS score, and 3-MWT distance ($P > 0.05$). However, baseline differences were observed for WOMAC pain, WOMAC stiffness, WOMAC physical function, total WOMAC score, GST, CST, and TUG ($P < 0.05$), indicating worse baseline clinical scores in the curcumin group.

Serum IL−1β and IL-6 levels

Serum IL-1β and IL-6 levels are presented in **Figure 1**. No significant changes were observed in the placebo group over the 4-week study period for either IL-1β ($P = 0.1465$) or IL-6 ($P = 0.1535$). In contrast, participants receiving curcumin showed significant reductions in both IL-1β ($P < 0.0001$) and IL-6 ($P < 0.05$) compared with baseline.

To further evaluate the treatment effect, changes from baseline were compared between groups (**Table 2**). The curcumin group showed significantly greater reductions in serum IL-1β ($P = 0.001$) and IL-6 ($P = 0.0282$) than the placebo group.

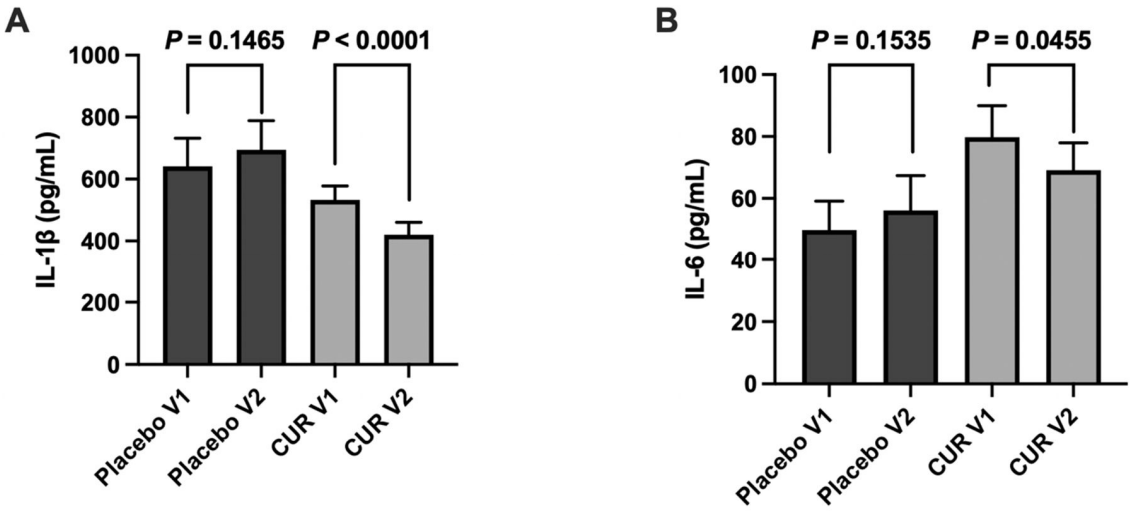


Figure 1. Inflammatory cytokine levels at baseline (V1) and week 4 (V2). (**A**) Serum IL-1β and (**B**) serum IL-6 levels. Values are presented as mean ± SEM. *P*-values indicate within-group comparisons between baseline (V1) and week 4 (V2) using the Wilcoxon matched-pairs signed-rank test. CUR, curcumin; IL, interleukin; SEM, standard error of the mean.

Table 2. Comparison of changes from baseline (Δ = week 4 − baseline) between the curcumin and placebo groups after 4 weeks of intervention

Outcomes	Curcumin Δ (Mean ± SEM)	Placebo Δ (Mean ± SEM)	*P*-value
IL-1β level (pg/mL)	−115.47 ± 31.89	+53.44 ± 61.92	0.001
IL-6 level (pg/mL)	−11.24 ± 4.08	+6.36 ± 4.46	0.0282
WOMAC (score)			
Pain	−5.06 ± 0.88	−0.68 ± 1.22	0.0038
Stiffness	−1.83 ± 0.48	+0.27 ± 1.05	0.0043
Function	−13.90 ± 2.59	+4.82 ± 3.02	<0.0001
Total	−20.79 ± 3.52	+4.41 ± 4.46	<0.0001
VAS (score)	−1.06 ± 0.25	−0.09 ± 0.46	0.0489
Physical performances			
3MWT (m)	+11.69 ± 3.90	+15.64 ± 5.98	0.9481
GST (m/s)	+0.14 ± 0.04	+0.00 ± 0.07	0.039
CST (s)	−2.15 ± 0.54	−1.45 ± 0.64	0.2057
TUG (s)	−1.01 ± 0.44	+0.21 ± 0.45	0.0174

Data are presented as mean ± SEM. Changes from baseline (Δ) were calculated as week 4 minus baseline. Between-group comparisons were performed using the Mann–Whitney *U* test. Statistical significance was defined as $P < 0.05$. 3MWT, 3-minutes walk test; CST, chair stand test; GST, gait speed test; IL, interleukin; SEM, standard error of the mean; TUG, timed up and go test; VAS, Visual Analog Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

WOMAC and VAS scores

Changes in WOMAC and VAS scores are shown in **Figure 2**. In the placebo group, no significant within-group changes were observed in WOMAC pain, stiffness, physical function, total WOMAC score, or VAS after 4 weeks. In contrast, the curcumin group demonstrated significant improvements in all WOMAC domains and VAS compared with baseline ($P < 0.001$).

Between-group comparison of changes from baseline (**Table 2**) showed significantly greater improvements in WOMAC pain ($P = 0.004$), WOMAC stiffness ($P = 0.004$), WOMAC physical function ($P < 0.0001$), total WOMAC score ($P < 0.001$), and VAS score ($P < 0.05$) in the curcumin group than in the placebo group.

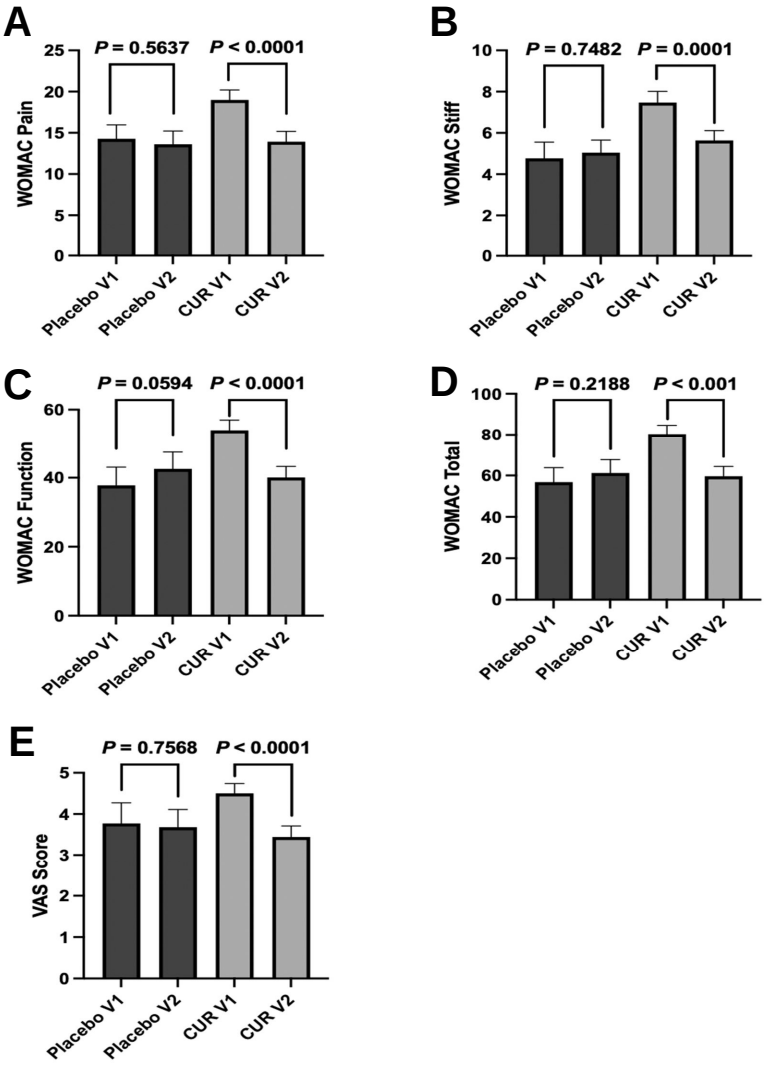


Figure 2. WOMAC and VAS scores at baseline (V1) and week 4 (V2). **(A)** WOMAC pain, **(B)** WOMAC stiffness, **(C)** WOMAC physical function, **(D)** WOMAC total score, and **(E)** VAS pain score. Values are presented as mean ± SEM. *P*-values indicate within-group comparisons between baseline (V1) and week 4 (V2) using the Wilcoxon matched-pairs signed-rank test. CUR, curcumin; SEM, standard error of the mean; VAS, Visual Analog Scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Functional mobility and physical functions

Physical performance outcomes are presented in **Figure 3**. In the placebo group, only the 3-MWT improved significantly after 4 weeks ($P = 0.0297$), whereas GST, CST, and TUG remained unchanged. In the curcumin group, significant improvements from baseline were observed in all physical performance measures, including the 3-MWT, GST, CST, and TUG ($P < 0.01$).

Comparison of changes from baseline between groups (**Table 2**) demonstrated significantly greater improvements in GST ($P = 0.039$) and TUG ($P = 0.0174$) in the curcumin group. In contrast, no significant differences between groups were observed for the 3-MWT or CST. These findings suggest that curcumin primarily improved gait-related performance and functional mobility rather than walking endurance or lower-limb strength.

Discussion

The present randomized controlled trial demonstrated that curcumin phytosome supplementation significantly reduced circulating IL-1β and IL-6 concentrations and improved pain, physical function, and selected mobility outcomes compared with placebo.

In the present study, treatment efficacy was assessed not only by within-group comparisons but also by comparing changes from baseline between the curcumin and placebo groups. This analysis reflects the treatment effect in randomized controlled trials, particularly when baseline differences are present. Despite higher baseline WOMAC scores and poorer functional performance in the curcumin group, participants receiving curcumin demonstrated significantly greater reductions in inflammatory cytokines and greater improvements in pain and functional outcomes than those receiving placebo.

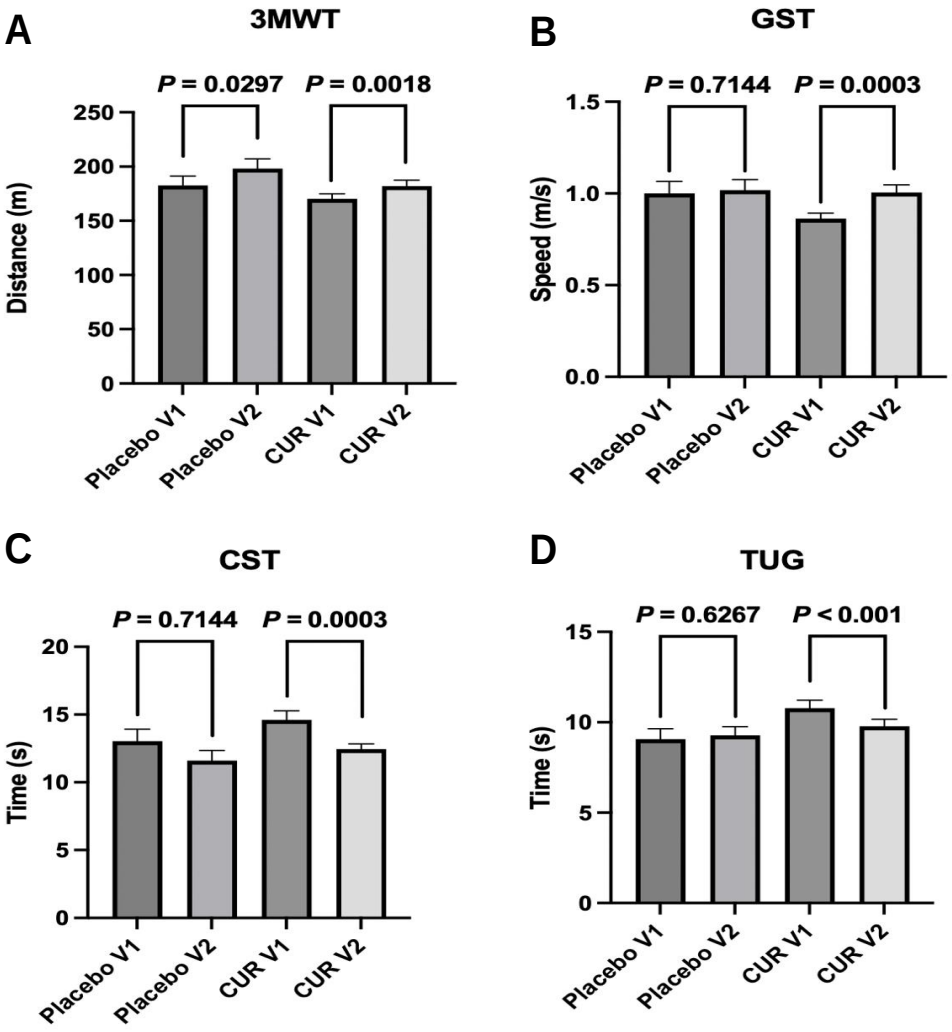


Figure 3. Physical performance measures at baseline (V1) and week 4 (V2). **(A)** 3-MWT, **(B)** GST, **(C)** CST, and **(D)** TUG test. Values are presented as mean ± SEM. *P*-values indicate within-group comparisons between baseline (V1) and week 4 (V2) using the Wilcoxon matched-pairs signed-rank test. 3MWT, 3-minute walk test; CST, chair stand test; GST, gait speed test; SEM, standard error of the mean; TUG, timed up and go.

The observed reduction in pro-inflammatory cytokines aligns with clinical evidence supporting curcumin's immunomodulatory effects in degenerative joint diseases. The reduction in circulating IL-1β and IL-6 levels observed in the present study is consistent with the findings reported [21], who documented progressive downregulation of IL-1β during prolonged curcumin supplementation. Similarly, the concurrent improvement in subjective pain scores and functional metrics measured using VAS and WOMAC is consistent with the non-inferiority trials. [3, 5] Those multicenter investigations demonstrated that curcuminoid extracts exhibited therapeutic efficacy comparable to that of standard NSAIDs such as ibuprofen.

Discrepancies appear, however, when these outcomes are compared with studies evaluating alternative drug delivery systems or lower dosage regimens. For instance, a prior clinical trial used a solid lipid curcumin particle formulation and reported significant pain relief but did not detect statistically significant changes in circulating cytokine levels. [20] This variance highlights how distinct formulation technologies influence systemic absorption and peripheral tissue distribution.

Furthermore, a prior clinical trial observed only a positive trend without statistical significance when adding standard curcumin extracts as an adjuvant to diclofenac therapy. [4] Differences between these clinical trials relate to several methodological factors: 1) Standard unformulated extracts require high daily doses (up to 2,000 mg) due to rapid intestinal metabolism and poor aqueous solubility. The utilization of a phytosome delivery system or specialized complexes, such as the BCM-95 formulation [22], enhances gastrointestinal absorption, enabling robust therapeutic responses at lower absolute doses. 2) The present cohort featured a high proportion of female participants and focused strictly on early-stage pathology (KL grade 1–2). Trials incorporating advanced radiographic joint space narrowing or older populations with extensive comorbidities often exhibit

higher baseline variance, masking subtle biomolecular shifts. 3) A 4-week timeframe captures acute biomolecular and symptomatic responses, whereas longer investigations (up to 120 days) track sustained disease-modifying trajectories but are prone to higher attrition rates and confounding rescue medication usage.

The concurrent improvement in inflammatory biomarkers and clinical outcomes observed in the present study is consistent with the recognized role of low-grade inflammation in KOA. Pro-inflammatory cytokines, particularly IL-1β and IL-6, have been implicated in synovial inflammation, pain sensitization, and functional impairment. Previous studies have demonstrated that elevated cytokine activity contributes to cartilage degradation and the progression of clinical symptoms. [2, 11] Therefore, the improvement in patient-reported outcomes and physical performance observed in this study may be partly associated with the attenuation of systemic inflammatory activity following curcumin supplementation.

Although significant within-group improvements were observed across all physical performance tests in the curcumin group, between-group comparisons showed significantly greater improvements only in gait speed and functional mobility, whereas no significant differences were observed for the 3-minute walk test or chair stand test. These findings indicate that short-term curcumin supplementation had a greater effect on gait performance and functional mobility than on walking endurance or lower-limb muscle endurance.

These findings are biologically plausible because previous experimental studies have shown that KOA is classified as a whole-joint disease driven by chronic, low-grade synovial inflammation rather than isolated mechanical wear. Upstream signaling cascades, specifically NF-κB and MAPK pathways, are activated in articular chondrocytes by mechanical loading and circulating adipokines. This activation prompts the transcription of critical pro-inflammatory cytokines, including IL-1β and IL-6.

Previous experimental studies have suggested that curcumin may interfere with IKK phosphorylation and NF-κB activation, thereby attenuating inflammatory signaling and reducing the expression of pro-inflammatory mediators. [23, 24] Modulation of these pathways has been associated with reduced expression of pro-inflammatory mediators, including IL-1β and IL-6.

The clinical relevance of these findings lies in the potential to optimize long-term pain management strategies for aging populations. Standard pharmacological management depends heavily on continuous oral NSAIDs. Chronic cyclooxygenase inhibition carries substantial systemic risks, such as gastrointestinal ulceration, renal impairment, and adverse cardiovascular events, which limit its safety in elderly patients with multiple comorbidities.

One strength of this study is that the methodology, which validates subjective patient-reported clinical indices (VAS and WOMAC) using timed, objective physical performance tests. Another strength of this study is the simultaneous evaluation of inflammatory biomarkers and objective functional outcomes, allowing biochemical changes to be interpreted alongside clinical improvement. Incorporating tests including the 3-MWT, GST, CST, and TUG provide a comprehensive overview of functional mobility, balance, and lower-limb muscular endurance, reducing the bias inherent to self-reported questionnaires. Additionally, the use of a phospholipid-complexed formulation addresses the traditional challenge of low curcumin bioavailability in clinical trials.

Limitations of the present study should be mentioned. First, the 4-week intervention period was sufficient to evaluate changes in inflammatory biomarkers and clinical symptoms but was not long enough to assess structural disease progression, such as radiographic changes in joint space narrowing. Second, while the single-blind design successfully minimized participant-side expectations, the lack of a double-blind setup might theoretically introduce observer variance, though this was strictly controlled by relying on objective physical performance tests (3-MWT, GST, CST, and TUG) and biochemical assays (IL-1β and IL-6). In addition, several clinical outcomes differed between groups at baseline despite randomization. To reduce the potential influence of these baseline differences, treatment effects were further evaluated by comparing changes from baseline between groups rather than relying solely on within-group comparisons. Third, the unequal distribution of participants between the treatment and control groups may have reduced the statistical power to detect subtle differences in certain secondary outcomes. Finally, the use of rescue medication (naproxen) on an as-needed basis may have introduced a potential confounding effect, although medication use was monitored throughout the study using participant diaries to minimize its influence on the study outcomes.

Future research should utilize longer, multi-center, double-blind designs with balanced cohorts to directly compare different advanced delivery systems, such as nano-micelles and solid lipid nanoparticles. Further studies should also determine long-term radiological outcomes and cartilage degradation biomarkers to fully substantiate any potential disease-modifying properties.

Conclusion

In summary, curcumin phytosome supplementation for four weeks resulted in greater reductions in serum IL-1β and IL-6 and greater improvements in pain, physical function, gait speed, and functional mobility than placebo in patients with primary knee osteoarthritis. Further randomized controlled trials with larger sample sizes and longer follow up are warranted.

Acknowledgements

The authors would like to express their sincere gratitude to all patients who participated in this study and to the nursing staff of the Department of Orthopaedics, King Chulalongkorn Memorial Hospital, for their invaluable assistance and support throughout the study. We also gratefully acknowledge the Organ Donation Center for providing facilities for placebo preparation. Special thanks are extended to Ms. Sinsuda Dechsupa for her guidance, support, and valuable advice during the conduct of this research. Furthermore, we appreciate Mr. Ron Chootapa and Mr. Yanapath Pullteap for their invaluable assistance with participant recruitment and study coordination.

This study was financially supported by the Thailand Science Research and Innovation Fund, Chulalongkorn University (Grant No. HEA_FF_68_088_3000_014), the 72nd Anniversary of His Majesty King Bhumibol Adulyadej Scholarship, Chulalongkorn University, and the 90th Anniversary of Chulalongkorn University Fund.

Conflict of interest statement

The authors declare no competing financial or personal interests.

Data sharing statement

Statistical summaries are presented in the published article. The data sets generated or analyzed during the present study are available from the corresponding author on reasonable request.

References

1. Global, regional, and national burden of osteoarthritis, 1990–2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Rheumatol 2023; 5: e508–22.
2. Jain SR, Baraskar SS, Shinde S. Effects of progressive neuromuscular control training on the functional mobility in stroke with bilateral osteoarthritic knee. Chula Med J 2025; 69:7–14.
3. Kuptniratsaikul V, Dajpratham P, Taechaarpornkul W, Buntragulpoontawee M, Lukkanapichonchut P, Chootip C, et al. Efficacy and safety of Curcuma domestica extracts compared with ibuprofen in patients with knee osteoarthritis: a multicenter study. Clin Interv Aging 2014; 9:451–8.
4. Pinsornsak P, Niempoog S. The efficacy of Curcuma longa L. extract as an adjuvant therapy in primary knee osteoarthritis: a randomized control trial. J Med Assoc Thai 2012; 95 Suppl 1:S51–8.
5. Kuptniratsaikul V, Thanakhumtorn S, Chinswangwatanakul P, Wattanamongkonsil L, Thamlikitkul V. Efficacy and safety of Curcuma domestica extracts in patients with knee osteoarthritis. J Altern Complement Med 2009; 15:891–7.
6. Tang S, Zhang C, Oo WM, Fu K, Risberg MA, Bierma-Zeinstra SM, et al. Osteoarthritis. Nat Rev Dis Primers 2025; 11:10.
7. Jarraya M, Guermazi A, Roemer FW. Osteoarthritis year in review 2023: Imaging. Osteoarthritis Cartilage 2024; 32:18–27.
8. Roelofs AJ, De Bari C. Osteoarthritis year in review 2023: Biology. Osteoarthritis Cartilage 2024; 32: 148–58.
9. Motta F, Barone E, Sica A, Selmi C. Inflammaging and osteoarthritis. Clin Rev Allergy Immunol 2023; 64: 222–38.
10. Coppola C, Greco M, Munir A, Musarò D, Quarta S, Massaro M, et al. Osteoarthritis: insights into diagnosis, pathophysiology, therapeutic avenues, and the potential of natural extracts. Curr Issues Mol Biol 2024; 46:4063–105.
11. Yao Q, Wu X, Tao C, Gong W, Chen M, Qu M, et al. Osteoarthritis: pathogenic signaling pathways and therapeutic targets. Signal Transduct Target Ther 2023; 8:56.
12. Anand P, Kunnumakkara AB, Newman RA, Aggarwal BB. Bioavailability of curcumin: problems and promises. Mol Pharm 2007; 4:807–18.
13. Xu XY, Meng X, Li S, Gan RY, Li Y, Li HB. Bioactivity, health benefits, and related molecular mechanisms of curcumin: current progress, challenges, and perspectives. Nutrients 2018; 10.
14. Wang Y, Fan M, Wang H, You Y, Wei C, Liu M, et al. Relative safety and efficacy of topical and oral NSAIDs in the treatment of osteoarthritis: a systematic review and meta-analysis. Medicine (Baltimore) 2022; 101:e30354.

15. LaForge JM, Urso K, Day JM, Bourgeois CW, Ross MM, Ahmadzadeh S, et al. Non-steroidal anti-inflammatory drugs: clinical implications, renal impairment risks, and AKI. Adv Ther 2023; 40: 2082–96.
16. Domper Arnal MJ, Hijos-Mallada G, Lanas A. Gastrointestinal and cardiovascular adverse events associated with NSAIDs. Expert Opin Drug Saf 2022; 21:373–84.
17. Coryell PR, Diekman BO, Loeser RF. Mechanisms and therapeutic implications of cellular senescence in osteoarthritis. Nat Rev Rheumatol 2021; 17:47–57.
18. Wang Z, Singh A, Jones G, Winzenberg T, Ding C, Chopra A, et al. Efficacy and safety of turmeric extracts for the treatment of knee osteoarthritis: a systematic review and meta-analysis of randomised controlled trials. Curr Rheumatol Rep 2021; 23:11.
19. Feng J, Li Z, Tian L, Mu P, Hu Y, Xiong F, et al. Efficacy and safety of curcuminoids alone in alleviating pain and dysfunction for knee osteoarthritis: a systematic review and meta-analysis of randomized controlled trials. BMC Complement Med Ther 2022; 22:276.
20. Gupte PA, Giramkar SA, Harke SM, Kulkarni SK, Deshmukh AP, Hingorani LL, et al. Evaluation of the efficacy and safety of Capsule Longvida® Optimized Curcumin (solid lipid curcumin particles) in knee osteoarthritis: a pilot clinical study. J Inflamm Res 2019; 12:145–52.
21. Srivastava S, Saksena AK, Khattri S, Kumar S, Dagur RS. Curcuma longa extract reduces inflammatory and oxidative stress biomarkers in osteoarthritis of knee: a four-month, double-blind, randomized, placebo-controlled trial. Inflammopharmacology 2016; 24: 377–88.
22. Shep D, Khanwelkar C, Gade P, Karad S. Efficacy and safety of combination of curcuminoid complex and diclofenac versus diclofenac in knee osteoarthritis: a randomized trial. Medicine (Baltimore) 2020; 99:e19723.
23. Qiu B, Xu X, Yi P, Hao Y. Curcumin reinforces MSC-derived exosomes in attenuating osteoarthritis via modulating the miR-124/NF-κB and miR-143/ROCK1/TLR9 signalling pathways. J Cell Mol Med 2020; 24:10855–65.
24. Chen W, Wang Q, Tao H, Lu L, Zhou J, Wang Q, et al. Subchondral osteoclasts and osteoarthritis: new insights and potential therapeutic avenues. Acta Biochim Biophys Sin (Shanghai) 2024; 56:499–512.