A Phase III Clinical Trial to Assess the Efficacy of Two Doses of Turmeric Powder on Joint Health and Muscle Strength in Subjects with Grade II Knee Osteoarthritis

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ABSTRACT

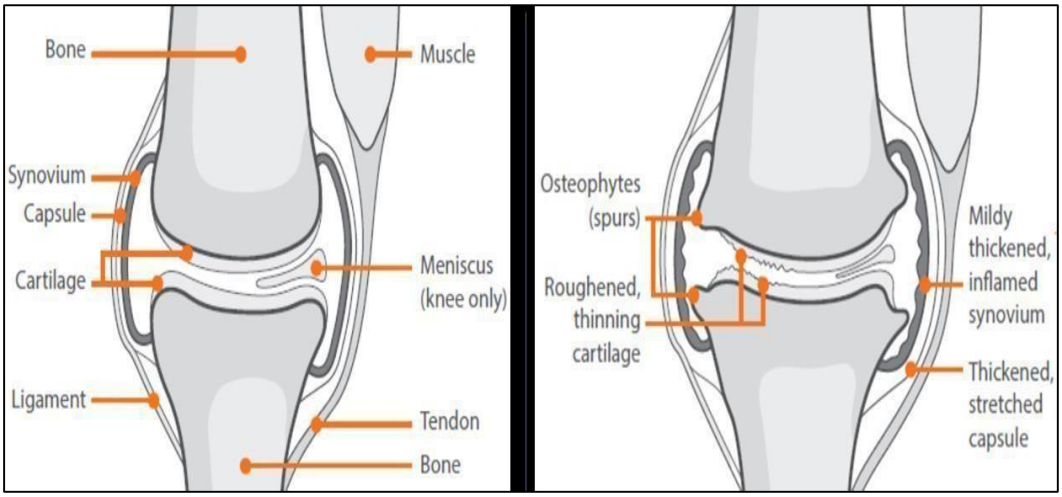
Osteoarthritis (OA) is a chronic degenerative joint disorder characterized by progressive cartilage degradation, pain, stiffness, and functional impairment. Knee osteoarthritis is one of the most prevalent forms of OA and significantly affects quality of life. Curcumin, the principal bioactive component of turmeric (Curcuma longa), possesses anti-inflammatory, antioxidant, and chondroprotective properties that may improve symptoms of osteoarthritis. To assess the efficacy and safety of two doses of turmeric powder on joint health and muscle strength in subjects with Grade II knee osteoarthritis.A prospective, randomized, double-blind, placebo-controlled, parallel-group Phase III clinical trial was conducted in 135 subjects diagnosed with Grade II knee osteoarthritis. Participants were randomized into three groups: Placebo, Turmeric Powder 250 mg, and Turmeric Powder 500 mg. Treatment was administered for 84 days. Clinical efficacy was evaluated using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Visual Analogue Scale (VAS), six-minute walk test (6MWT), hand-held dynamometry (HHD), range of motion (ROM), and inflammatory biomarkers including hs-CRP and IL-1β.Both turmeric treatment groups demonstrated significant improvements in WOMAC scores, pain reduction, physical function, muscle strength, and inflammatory markers compared with placebo. The 500 mg turmeric group exhibited greater efficacy than the 250 mg group throughout the treatment period. Turmeric supplementation significantly improved joint health and muscle strength in subjects with Grade II knee osteoarthritis. The higher dose demonstrated superior clinical benefits and was well tolerated.

Keywords

Turmeric, Curcumin, Osteoarthritis, WOMAC, Knee Pain, Inflammation, Clinical Trial

INTRODUCTION

Osteoarthritis is a chronic degenerative joint disorder characterized by progressive cartilage degradation, joint pain, stiffness, and reduced mobility. It is one of the leading causes of disability among older adults worldwide and significantly affects quality of life. The prevalence of osteoarthritis continues to increase due to aging populations, obesity, and sedentary lifestyles. The knee joint is among the most commonly affected sites, resulting in pain during walking, climbing stairs, and other daily activities. Osteoarthritis is a progressive degenerative joint disease affecting millions of individuals worldwide. It is characterized by cartilage degeneration, subchondral bone remodeling, osteophyte formation, pain, stiffness, and reduced joint mobility. Knee osteoarthritis represents one of the most common causes of disability among elderly individuals. [1,2]



Pathophysiology of Osteoarthritis

The pathogenesis of osteoarthritis involves inflammatory mediators such as interleukin-1 beta (IL-1β), tumor necrosis factor-alpha (TNF-α), cyclooxygenase enzymes, and matrix metalloproteinases. These mediators contribute to cartilage degradation and progression of joint damage.

Osteoarthritis involves the breakdown of articular cartilage, subchondral bone remodeling, synovial inflammation, and osteophyte formation. Inflammatory mediators such as interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), and various matrix metalloproteinases contribute to cartilage destruction and disease progression. Oxidative stress also plays a significant role in damaging chondrocytes and extracellular matrix components. [3,4]

Limitations of Conventional Therapy

Current treatment strategies for osteoarthritis mainly focus on symptom relief through analgesics, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and physical therapy. Although these therapies can reduce pain, long-term use may be associated with gastrointestinal, renal, and cardiovascular adverse effects. Consequently, there is growing interest in safer and more effective alternative therapies. Considering its favorable safety profile and multiple pharmacological actions, turmeric supplementation may represent an effective therapeutic option for osteoarthritis management. [5,6]

Curcumin: A Natural Therapeutic Agent

Curcumin is the principal bioactive compound obtained from the rhizome of Curcuma longa. It has been extensively studied for its anti-inflammatory, antioxidant, antimicrobial, and immunomodulatory properties. Curcumin can modulate multiple molecular targets involved in inflammation and oxidative stress, making it a promising candidate for osteoarthritis management. [7,8]

Turmeric (Curcuma longa) has been used traditionally in Ayurvedic medicine for centuries. Curcumin, the major polyphenolic constituent of turmeric, possesses anti-inflammatory, antioxidant, antimicrobial, and analgesic properties. Recent studies have demonstrated that curcumin inhibits NF-κB activation, suppresses inflammatory cytokines, and protects articular cartilage from degeneration.

Curcumin suppresses inflammatory pathways by inhibiting nuclear factor-kappa B (NF-κB), cyclooxygenase-2 (COX-2), lipoxygenase (LOX), and pro-inflammatory cytokines such as IL-1β and TNF-α. Through these mechanisms, curcumin may reduce synovial inflammation and slow cartilage degradation. [9,10]

Oxidative stress contributes significantly to osteoarthritis progression. Curcumin acts as a potent antioxidant by scavenging free radicals and enhancing endogenous antioxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. This protective effect may help preserve chondrocyte viability and joint integrity. [11,12]

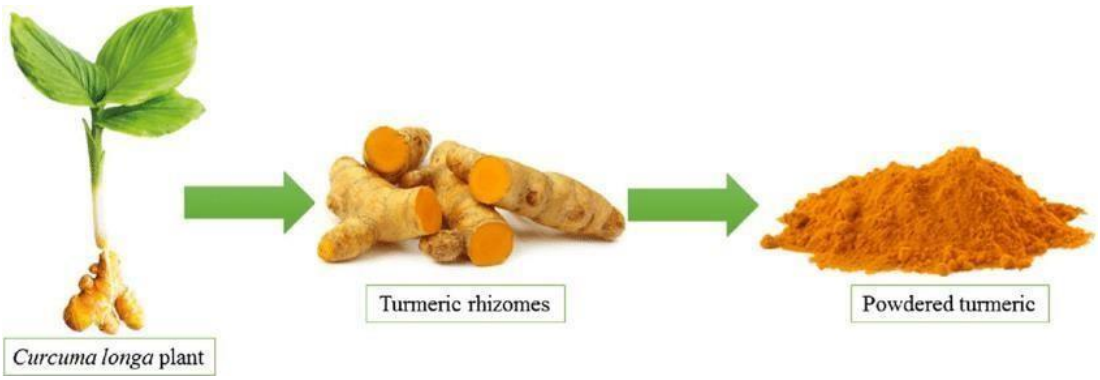


Figure 2: Picture of botanical source of Turmeric

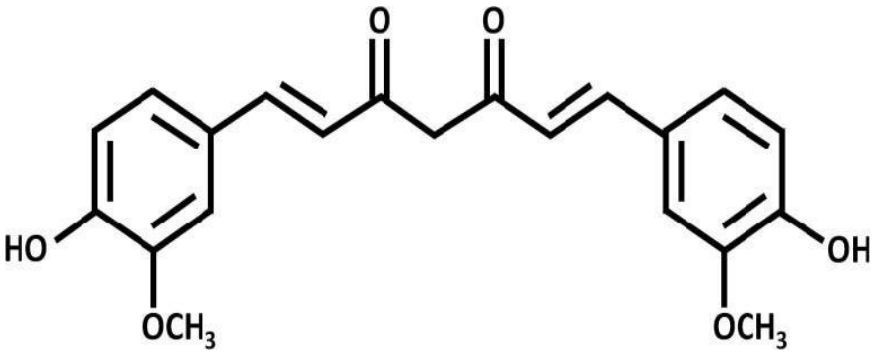


Figure 3: Chemical Structure of Turmeric

Clinical Benefits in Osteoarthritis

Several clinical studies have reported that curcumin supplementation may improve pain, stiffness, physical function, and overall quality of life in patients with knee osteoarthritis. Improvements are often measured using standardized tools such as the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) score. Curcumin has also shown potential for improving muscle strength and mobility when used consistently over time. [13–15]

Curcumin is generally considered safe and well tolerated when administered in appropriate doses. Reported adverse effects are usually mild and may include gastrointestinal discomfort, nausea, or diarrhea. Compared with long-term NSAID therapy, curcumin may offer a favorable safety profile for chronic use. [16,17]

Despite promising findings, variability in curcumin formulations, bioavailability, dosage, and study design has limited the establishment of definitive clinical guidelines. Well-designed randomized controlled trials are needed to determine the optimal dose, duration, and formulation of curcumin for osteoarthritis management. [18,19]

Osteoarthritis is a major public health concern associated with chronic pain and functional impairment. Curcumin possesses significant anti-inflammatory and antioxidant properties that may help improve symptoms, joint function, and muscle strength in individuals with osteoarthritis. Emerging evidence supports

its potential role as a complementary therapeutic option; however, further large-scale clinical studies are required to confirm its long-term efficacy and safety. [20]

METHODOLOGY

Study Design

A prospective, randomized, double-blind, placebo-controlled Phase III clinical trial was conducted to evaluate the efficacy and safety of two doses of curcumin powder in subjects diagnosed with Grade II knee osteoarthritis. The study was designed in accordance with the principles of Good Clinical Practice (GCP), the Declaration of Helsinki, and applicable regulatory guidelines. Randomization and double-blinding were employed to minimize bias and ensure the reliability of study outcomes. [21,22]

Study Population

A total of 135 subjects with clinically and radiographically confirmed Grade II knee osteoarthritis were enrolled in the study. Eligible participants were men and women aged between 40 and 75 years who experienced persistent knee pain and fulfilled the diagnostic criteria for osteoarthritis. Subjects with severe osteoarthritis, inflammatory joint diseases, recent knee surgery, or serious systemic illnesses were excluded from participation. [23]

Randomization and Blinding

The enrolled subjects were randomly assigned in a 1:1:1 ratio into three treatment groups consisting of 45 subjects each. Randomization was performed using a computer-generated random allocation sequence. Both participants and investigators remained blinded to treatment allocation throughout the study period. Study medications and placebo capsules were identical in appearance, packaging, and labeling to maintain blinding. [24]

Treatment Groups

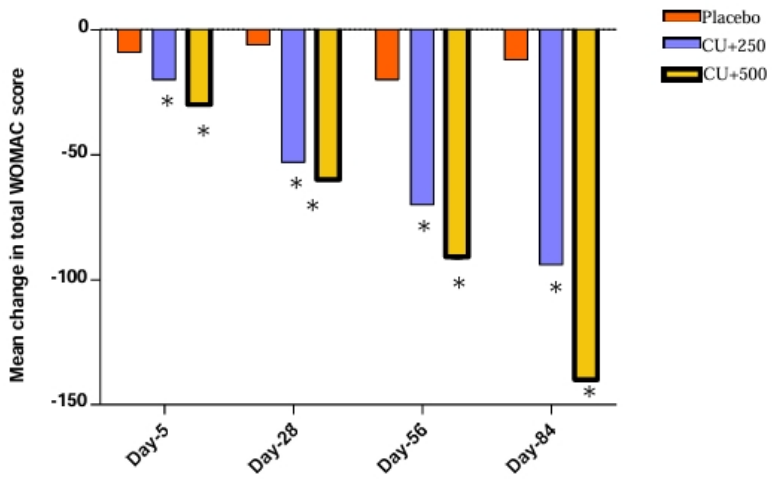


Figure 4: Mean Change from Baseline in Total WOMAC Score between Treatment Groups.

Participants were allocated to one of the following treatment groups:

Group I – Placebo Group

Subjects received placebo capsules once daily for 84 days.

Group II – Curcumin 250 mg Group

Subjects received curcumin powder 250 mg orally once daily for 84 days.

Group III – Curcumin 500 mg Group

Subjects received curcumin powder 500 mg orally once daily for 84 days.

Compliance with treatment was monitored through capsule counts and patient diaries during follow-up visits. [25]

Study Duration

The total duration of treatment and observation was 84 days (12 weeks). Subjects attended scheduled visits at baseline and at predetermined intervals during the study period. Clinical assessments and safety evaluations were performed at each visit to monitor treatment response and adverse events. [26]

Efficacy Assessment

The primary objective of the study was to assess the effect of curcumin supplementation on joint health and muscle strength in subjects with Grade II knee osteoarthritis.

Primary Endpoints

- Change in knee pain score from baseline.
- Change in WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) score.
- Improvement in joint stiffness.
- Improvement in physical function and mobility.
- Enhancement of muscle strength and endurance.

Secondary Endpoints

- Reduction in inflammation-related symptoms.
- Improvement in quality of life.
- Reduction in the requirement for rescue medication.
- Overall patient and investigator assessment of treatment efficacy. [27,28]

Safety Assessment

Safety evaluations were conducted throughout the study by monitoring adverse events, vital signs, physical examinations, and laboratory investigations. Hematological, biochemical, and urine analyses were performed at baseline and at the end of the study. Any adverse event reported during the trial was documented and assessed for severity and relationship to the study medication. [29]

Data Collection

Clinical data were collected using standardized case report forms (CRFs). Information regarding demographic characteristics, medical history, concomitant medications, efficacy assessments, laboratory findings, and adverse events was systematically recorded. Data quality was ensured through regular monitoring and verification procedures. [30]

Statistical Analysis

Statistical analysis was performed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Comparisons between treatment groups were conducted using analysis of variance (ANOVA) followed by suitable post-hoc tests. Within-group comparisons from baseline to the end of treatment were analyzed using paired statistical tests. A p-value of less than 0.05 was considered statistically significant. [31,32]

Ethical Considerations

The study protocol was reviewed and approved by an Institutional Ethics Committee prior to initiation. Written informed consent was obtained from all participants before enrollment. Confidentiality of participant information was maintained throughout the study, and subjects were free to withdraw from the trial at any time without prejudice. [33]

In summary, this study employed a prospective randomized double-blind placebo-controlled design involving 135 subjects with Grade II knee osteoarthritis. Participants received placebo, curcumin 250 mg, or curcumin 500 mg for 84 days. Clinical efficacy was assessed through pain, WOMAC scores, joint function, and muscle strength evaluations, while safety was monitored through adverse event reporting and laboratory investigations. The study aimed to determine the effectiveness of curcumin supplementation in improving joint health and functional outcomes in osteoarthritis patients. [21–33]

RESULTS

The efficacy of curcumin supplementation was evaluated in subjects with Grade II knee osteoarthritis over a treatment period of 84 days. Clinical outcomes were assessed using pain scores, WOMAC scores, physical function parameters, muscle strength measurements, and inflammatory biomarkers. Both curcumin-treated groups demonstrated statistically significant improvements compared with the placebo group throughout the study period.

Table 1: Demographic and Baseline Characteristics

Parameter	Test Product 1	Test Product 2	Placebo
Age (Years)	51.89 ± 9.27	51.38 ± 11.52	53.09 ± 9.30
Number of Subjects	45	45	45
Weight (kg)	65.28 ± 10.24	65.78 ± 11.93	65.40 ± 8.59
BMI (kg/m²)	25.69 ± 4.23	25.88 ± 4.88	25.79 ± 3.56

Improvement in WOMAC Score

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score was used to assess pain, stiffness, and physical function. Subjects receiving curcumin exhibited a significant reduction in total WOMAC scores compared with baseline values. The reduction was greater in the 500 mg curcumin group than in the 250 mg group, indicating a dose-dependent therapeutic effect. The placebo group showed only minimal changes during the study period.

Table 2: Mean Change in WOMAC Score

Visit	Placebo	Turmeric 250 mg	Turmeric 500 mg
Day 5	Minimal	Significant	Greater Significant
Day 28	Moderate	Significant	Highly Significant
Day 56	Moderate	Significant	Highly Significant
Day 84	Moderate	Significant	Maximum Improvement

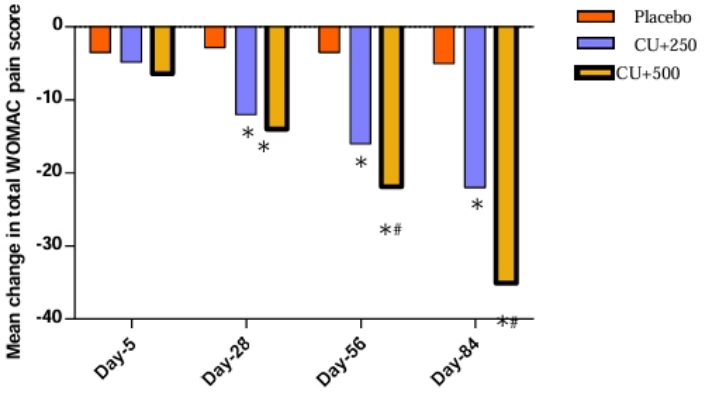


Figure 5: Mean Change from Baseline in WOMAC Pain Score between Treatment Groups.

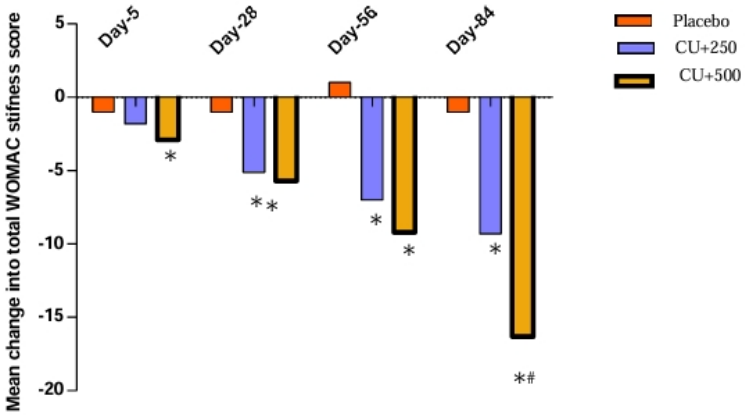


Figure 6: Mean Change from Baseline in WOMAC Stiffness Score between Treatment Groups

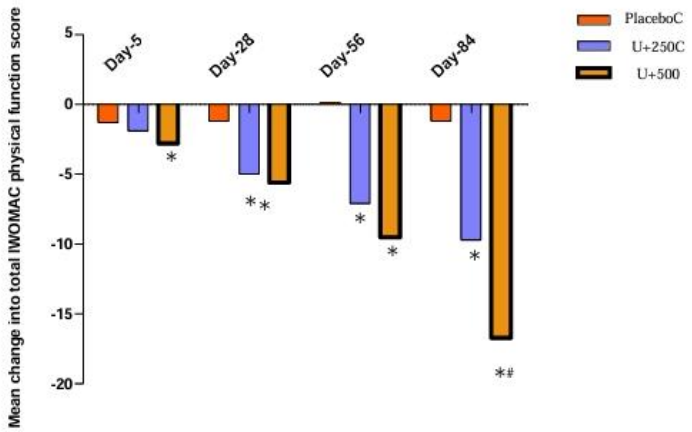


Figure 7: Mean Change from Baseline in WOMAC Physical Function Score between Treatment Groups

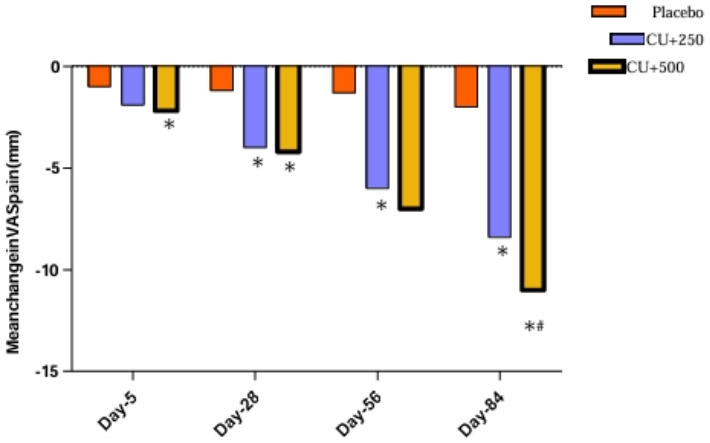


Figure 8: Mean Change from Baseline in VAS Pain Score between Treatment Groups

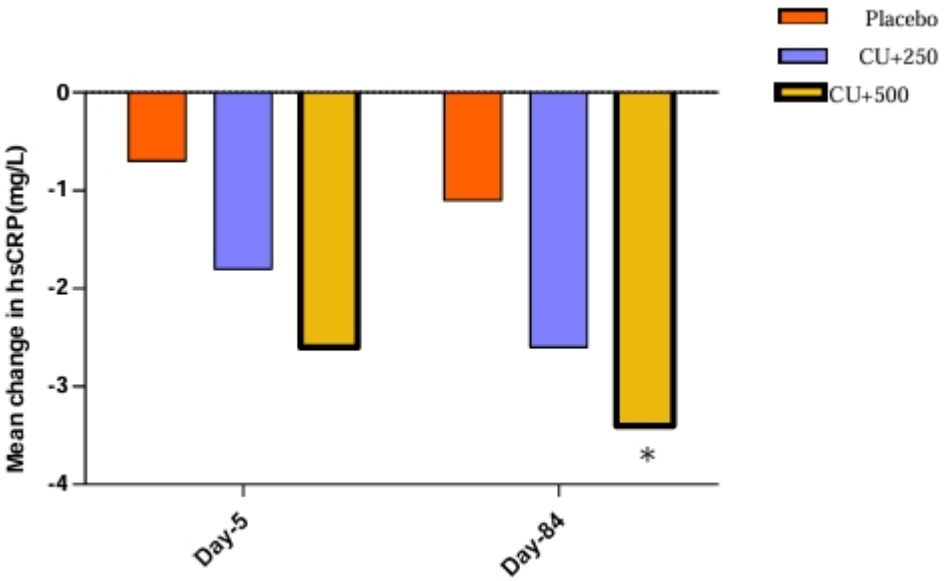


Figure 9: Mean Change from Baseline in hsCRP Levels between Treatment Groups.

Reduction in Pain Severity

A significant decrease in knee pain severity was observed among subjects receiving curcumin supplementation. Improvements became evident during follow-up visits and continued throughout the treatment period. The 500 mg curcumin group demonstrated the greatest reduction in pain scores, followed by the 250 mg group, while the placebo group exhibited comparatively limited improvement.

Improvement in Physical Function

Physical function assessments revealed marked enhancement in mobility, walking ability, and performance of daily activities among participants treated with curcumin. Subjects reported reduced difficulty in climbing stairs, standing from a seated position, and walking for extended periods. The highest improvement was observed in the 500 mg curcumin group, suggesting superior efficacy at the higher dose.

Enhancement of Muscle Strength

Muscle strength and endurance improved significantly in both curcumin treatment groups. Participants demonstrated better lower-limb functional performance and reduced fatigue during physical activities. The improvement was more pronounced in subjects receiving 500 mg of curcumin compared with those receiving 250 mg.

Effect on Inflammatory Parameters

Curcumin supplementation was associated with a reduction in inflammatory markers related to osteoarthritis progression. The anti-inflammatory activity of curcumin contributed to improved joint comfort and functional outcomes. Subjects receiving the higher dose exhibited greater reductions in inflammation-related parameters than those receiving the lower dose.

Comparison between Treatment Groups

Placebo Group

- Minimal improvement in pain and functional scores.
- No significant changes in inflammatory parameters.
- Limited overall clinical benefit.

Curcumin 250 mg Group

- Significant reduction in pain scores.
- Improvement in WOMAC score and physical function.
- Better muscle strength and mobility compared with placebo.

Curcumin 500 mg Group

- Greatest reduction in pain and stiffness.
- Maximum improvement in WOMAC score.
- Superior enhancement of physical function and muscle strength.
- Most significant reduction in inflammatory markers.

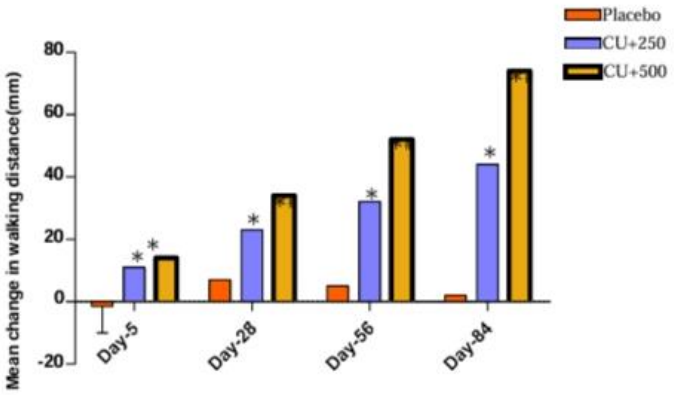


Figure 10: Mean Change from Baseline in Six-Minute Walk Distance between Treatment Groups

Safety Outcomes

Both doses of curcumin were well tolerated throughout the study. No serious adverse events related to the study medication were reported. Laboratory investigations, vital signs, and clinical assessments remained within acceptable limits, indicating a favorable safety profile for curcumin supplementation.

Statistical Significance

Statistical analysis demonstrated that improvements observed in both curcumin treatment groups were significantly greater than those observed in the placebo group ($p < 0.05$). The 500 mg dose consistently produced superior outcomes across all efficacy parameters, indicating a dose-dependent respo

The study demonstrated that curcumin supplementation significantly improved clinical symptoms and functional outcomes in subjects with Grade II knee osteoarthritis. Both the 250 mg and 500 mg doses were effective; however, the 500 mg dose consistently produced superior improvements in WOMAC score, pain reduction, physical function, muscle strength, and inflammatory parameters. These findings support the potential role of curcumin as a safe and effective therapeutic option for the management of knee osteoarthritis.

DISCUSSION

The present study demonstrated that turmeric supplementation significantly improved symptoms and physical performance in subjects with Grade II knee osteoarthritis. Improvements were observed in pain reduction, joint stiffness, physical function, and muscle strength. The anti-inflammatory activity of curcumin likely contributed to the reduction in hs-CRP and IL-1β levels.

The superior performance of the 500 mg dose suggests a dose-dependent therapeutic response. These findings are consistent with previous clinical studies demonstrating beneficial effects of curcumin in osteoarthritis management.

The findings of the present study demonstrate that curcumin supplementation significantly improved clinical outcomes in subjects with Grade II knee osteoarthritis. Both the 250 mg and 500 mg curcumin doses produced beneficial effects compared with placebo; however, the 500 mg dose consistently resulted in superior improvements in pain reduction, WOMAC scores, physical function, muscle strength, and inflammatory

parameters. These observations suggest a dose-dependent therapeutic effect of curcumin in the management of knee osteoarthritis.

Effect of Curcumin on Osteoarthritis Symptoms

Osteoarthritis is characterized by chronic pain, joint stiffness, reduced mobility, and progressive cartilage degeneration. The significant reduction in pain and improvement in joint function observed in the present study indicate that curcumin may effectively alleviate the clinical symptoms associated with osteoarthritis. These findings are consistent with previous clinical investigations that reported improved functional outcomes and reduced pain following curcumin supplementation.

Anti-inflammatory Activity of Curcumin

One of the primary mechanisms underlying the beneficial effects of curcumin is its potent anti-inflammatory activity. Curcumin has been shown to inhibit the activation of nuclear factor-kappa B (NF-κB), cyclooxygenase-2 (COX-2), tumor necrosis factor-alpha (TNF-α), and interleukin-1 beta (IL-1β), all of which play critical roles in osteoarthritis progression. Suppression of these inflammatory mediators may reduce synovial inflammation and prevent further cartilage destruction, thereby improving joint health and function.

Antioxidant Properties and Joint Protection

Oxidative stress contributes significantly to cartilage degradation and disease progression in osteoarthritis. Curcumin possesses strong antioxidant properties that enable it to neutralize reactive oxygen species and enhance endogenous antioxidant defense systems. The observed clinical improvements may therefore be partly attributed to the reduction of oxidative damage within the joint environment. Protection of chondrocytes from oxidative stress may contribute to preservation of cartilage integrity and improved joint performance.

Improvement in Physical Function and Muscle Strength

The enhancement in physical function and muscle strength observed among subjects receiving curcumin supplementation is clinically important. Reduced pain and inflammation likely enabled participants to engage more effectively in daily activities and movement. Improved muscle strength may further contribute to joint stability and reduced mechanical stress on the affected knee joint. The greater improvements observed in the 500 mg group suggest that higher doses may provide additional functional benefits.

Dose-Dependent Therapeutic Response

Comparison between treatment groups revealed that the 500 mg curcumin dose consistently produced greater improvements than the 250 mg dose across all measured efficacy parameters. This dose-dependent response indicates that higher concentrations of curcumin may provide enhanced anti-inflammatory and antioxidant effects, resulting in superior clinical outcomes. Nevertheless, both doses were effective and well tolerated throughout the study period.

Comparison with Previous Studies

The results of the present investigation are in agreement with several previously published studies that have demonstrated the effectiveness of curcumin in reducing pain and improving function in osteoarthritis patients. Earlier clinical trials have reported significant improvements in WOMAC scores, pain severity, and quality of

life following curcumin administration. The findings of this study further strengthen the evidence supporting curcumin as a promising complementary therapy for osteoarthritis management.

Safety and Tolerability

An important observation of the present study was the favorable safety profile of curcumin. No serious adverse events related to the study medication were reported, and both doses were generally well tolerated. These findings support previous reports indicating that curcumin is safe for long-term use and may represent a suitable alternative or adjunct to conventional anti-inflammatory therapies that are often associated with significant adverse effects.

Study Limitations

Although the study demonstrated encouraging results, several limitations should be acknowledged. The duration of treatment was limited to 84 days, and longer follow-up periods may be necessary to evaluate sustained therapeutic effects. In addition, the study included only subjects with Grade II knee osteoarthritis, which may limit generalization of the findings to patients with more advanced disease. Future studies involving larger populations and extended treatment durations are warranted. [43]

Clinical Significance

The significant improvements observed in pain, joint function, muscle strength, and inflammatory parameters indicate that curcumin may offer a valuable therapeutic option for patients with knee osteoarthritis. Its multi-targeted mechanism of action, combined with its favorable safety profile, makes curcumin an attractive candidate for long-term management of osteoarthritis symptoms and functional impairment.

The results of the present study support previous evidence that curcumin exerts anti-inflammatory, antioxidant, and chondroprotective effects in subjects with knee osteoarthritis. The observed improvements in clinical outcomes may be attributed to suppression of inflammatory mediators, reduction of oxidative stress, and preservation of joint function. Among the evaluated doses, curcumin 500 mg demonstrated the greatest therapeutic benefit, suggesting that higher-dose supplementation may provide superior efficacy in the management of Grade II knee osteoarthritis.

CONCLUSION

Turmeric powder supplementation was effective and safe in improving joint health and muscle strength among subjects with Grade II knee osteoarthritis. The 500 mg dose demonstrated superior efficacy compared with the 250 mg dose. Turmeric may serve as a valuable adjunctive therapy in osteoarthritis management. Curcumin is a safe and effective intervention for subjects with Grade II knee osteoarthritis. It significantly improves pain, joint function, muscle strength, and overall quality of life through its anti-inflammatory and antioxidant properties. The 500 mg dose demonstrated greater efficacy than the 250 mg dose. These findings suggest that curcumin may serve as a valuable adjunct or alternative to conventional osteoarthritis therapy with a favorable safety profile.

FUTURE SCOPE

Future research should focus on evaluating the long-term efficacy and safety of curcumin supplementation in patients with knee osteoarthritis. Studies involving radiographic assessment of joint structure and disease progression would provide valuable insights into its potential disease-modifying effects. Additionally,

investigating the combined use of curcumin with physiotherapy, exercise programs, and other non-pharmacological interventions may help optimize clinical outcomes. Further clinical trials are also needed to assess the effectiveness of curcumin in patients with advanced stages of osteoarthritis. Moreover, the development and evaluation of bioavailability-enhanced curcumin formulations could improve therapeutic efficacy and maximize its clinical benefits in osteoarthritis management formulations.

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