Safety and Efficacy of Turmeric (*Curcuma longa*) Extract and Curcumin Supplements in Musculoskeletal Health: A Systematic Review and Meta-Analysis

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**ABSTRACT**

**Context**: Turmeric is a well-known herb that has been used in many traditional medicinal systems since ancient times. Turmeric roots contain hydrophobic polyphenols called curcuminoids, which have proven anti-inflammatory and antioxidant effects and are shown to be beneficial for the management of musculoskeletal health. Various products containing curcumin or turmeric extract are commercially available.

**Objective**: This systematic review and meta-analysis of randomized clinical trials (RCTs) is intended to evaluate the effective dose, safety, and efficacy of commercial turmeric extract and curcumin supplements in musculoskeletal health.

**Design**: The research team performed a systematic literature search of PubMed, Google Scholar, and Cochrane Library databases and conducted a meta-analysis according to PRISMA guidelines.

**Setting**: Authors from India and USA contributed to this systematic review and meta-analysis.

**Results**: The research team analyzed 21 prospective, randomized clinical studies, of which seven studies were focused on skeletal muscle health and fourteen on joint health. Statistical heterogeneity was established based on the results of heterogeneity analysis of a Chi-square (χ²) value for Cochran’s Q statistic of 29.3765 for musculoskeletal and 3666.80 for joint health studies (P < .0001 for both analyses). Therefore, the random effects model was used. The χ² value of the random effects model was 216.5545 for skeletal muscle health studies and 1400.65 for joint health studies, which was statistically significant with P < .0001 for both analyses.

**Conclusions**: Turmeric extract and curcumin supplements can be effective adjuvants for the management of musculoskeletal health, with a low incidence of AEs. The water-dispersible turmeric extract, WDTE60N, at a dose of 250 mg per day, was found to be more effective than other curcumin products. However, the studies included in the analysis were conducted using diverse doses and treatment durations. Further evaluation using comparisons in future clinical trials can establish the appropriate effective dose of curcumin supplements for the overall maintenance of musculoskeletal health. (*Altern Ther Health Med.* 2023;29(6):12-24).

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Botanicals and herbs have been used throughout human history for consumption as delicacies, and more important, for their health benefits, owing to their biological or pharmacological applications. Many of these herbs and botanicals have been extensively studied, with increasing evidence of their therapeutic applications and health benefits, and they are considered valuable ingredients in the nutraceutical sector.

The term nutraceuticals refers to specialized foods or food-derived products that provide health and medical benefits, including the prevention and treatment of diseases,
Curcuma longa is a rhizomatous, herbaceous, perennial herb belonging to the ginger family and has a broad variety of biological properties, such as antioxidant, anti-inflammatory, antimutagenic, antimicrobial, and anticancer properties. These properties belong to the bioactive principles in the rhizomes, the hydrophobic polyphenols called curcuminoids, which comprise curcumin, demethoxycurcumin, and bisdemethoxycurcumin, of which curcumin—1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione—is the major natural polyphenol.

Curcuminoids, commonly called curcumin, have been shown to exhibit a broad spectrum of pharmacological actions proven in several in-vitro and in-vivo studies as well as in clinical trials. Curcumin has also been recognized as safe by the US Food and Drug Administration (FDA).

The musculoskeletal system relates to an individual's mobility and dexterity. It comprises muscles, bones, joints, and adjacent connective tissue. It plays a major role in mobility and is important in maintaining an active, productive, and prolonged working life. Common musculoskeletal conditions that often hamper the body's mobility include osteoarthritis (OA), rheumatoid arthritis (RA), lower back pain (LBP), and osteoporosis (OP) as well as acute conditions, such as delayed onset muscle soreness (DOMS).

DOMS is a constellation of muscular pain and stiffness that occurs in healthy individuals several hours after undergoing unaccustomed exercise. It is caused by eccentric muscle activity associated with inflammatory responses and the production of reactive oxygen species (ROS) that cause inflammation and oxidative stress. Musculoskeletal disorders cause the highest global burden on individuals, health, and social-care systems. According to the Global Burden of Disease (GBD) Study, as of 2019, 1.71 billion cases of musculoskeletal disorders have been reported globally. Lower back pain was the most prevalent (36.8%), followed by other musculoskeletal disorders (21.5%), OA (19.3%), neck pain (18.4%), gout (2.6%), and RA (1.3%).

According to the World Health Organization (WHO) statement in July 2022, musculoskeletal conditions, along with increasing the risk in non-communicable diseases, are also the highest contributor to the global need for rehabilitation, which accounts for approximately two-thirds of all adults in need of rehabilitation. Individuals with musculoskeletal conditions are also at a higher risk of developing mental health issues.

According to a systematic analysis of the Global Burden of Disease Study, as of 2015, musculoskeletal disorders were a leading cause of disability worldwide and a long-term burden from the sequelae of fractures and dislocations. Considering these data, effective management of musculoskeletal diseases is important.

The first-line management of musculoskeletal health conditions includes analgesics, such as paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs). However, these drugs have low and transient analgesic effects, and several studies have observed AEs, especially in senior patients with pre-existing comorbidities. In particular, the safety of NSAIDs remains a concern when selecting a dose regimen for patients.

The long-term use of NSAIDs can cause gastrointestinal disorders, such as dyspepsia, ulcers, bleeding, and perforation as well as cardiovascular, and kidney problems. These factors contribute to the increased need for alternative options for managing musculoskeletal conditions, such as dietary supplements and natural products.

Curcumin is one such option that has shown the potential for improving musculoskeletal health due to its anti-inflammatory action, as observed in many in-vitro and in-vivo studies as well as in clinical trials. Curcumin has demonstrated efficacy in reducing the impact of DOMS, as suggested by its effects on pain intensity and muscle injury, and its anti-arthritic effects, include inhibition of joint inflammation and periarticular joint destruction.

Mechanism of Action
Curcumin is a pleiotropic molecule that has multiple mechanisms of action. It inhibits mRNA expression of inflammatory mediators, including interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), and matrix metalloproteinases (MMPs), which play an important role in musculoskeletal disorders through various pathways.

Curcumin alters enzyme activities, growth factor receptors, co-factors, and other molecules, including protecting IL-1β-induced apoptotic chondrocytes, decreasing the early degenerative changes of articular cartilage, and inhibiting cytoplasmic phospholipase A2 (cPLA2), cyclooxygenase 2 (COX-2), and 5-lipoxygenase (5-LOX) pathways.

Curcumin helps reduce muscle pain and muscle damage, as evidenced by the reduction in lactate dehydrogenase (LDH) levels and ensures faster muscle recovery. It exerts an anti-inflammatory effect by modulating pro-inflammatory cytokines, such as TNF-α, IL-6, and IL-8, and exerts an antioxidant effect.

Current Review and Meta-analysis
This systematic review and meta-analysis of randomized clinical trials (RCTs) is intended to evaluate the effective dose, safety, and efficacy of commercial turmeric extract and curcumin supplements in musculoskeletal health.

METHODS

Procedures
The data for this meta-analysis were reviewed and analyzed by the authors from India and the USA.

Search strategy and selection criteria. The research team performed the systematic review by searching PubMed,
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Google Scholar, and Cochrane Library databases and conducted a meta-analysis according to PRISMA guidelines.18 The review and meta-analysis included studies if they: (1) were prospective RCTs; (2) evaluated the safety, efficacy, and effective dose of curcumin for musculoskeletal health; and (3) recruited participants older than 18 years of age who were either healthy or had reported musculoskeletal disorders.

The review and meta-analysis excluded studies if they used no musculoskeletal health indications, or if they used a study design other than RCT.

As search terms, the electronic searches used medical subject headings (MeSH) terms and the corresponding keywords. The search terms used were (MeSH “Curcuma,” “Curcumin” and keywords “curcuma,” “turmeric,” “turmeric extract,” “curcumin,” “curcuminoid”), and (MeSH “Arthritis,” “Osteoarthritis,” “knee osteoarthritis,” “rheumatoid arthritis” and the keywords were “arthritis,” “osteoarthritis,” “musculoskeletal disorders,” “DOMS,” “muscle soreness”).

Additionally, the research team manually checked the bibliographies of the identified articles, including relevant systematic reviews and meta-analyses, to identify additional eligible studies.

Search
The research team identified 1540 records through Google Scholar, followed by 370 from PubMed and 73 from Cochrane database. Forty-two records were included after removing duplicates, of which 23 were excluded because they didn’t meet the required criteria. Ultimately, 19 prospective RCTs were included in this systematic review and meta-analysis (Figure 1).

Of those 19 prospective RCTs that evaluated the efficacy and safety of curcumin, seven studies were related to skeletal muscle health and 12 studies were related to joint conditions.

Muscle Health: Systematic Review
Table 1 shows the characteristics of the included studies.21

Mallard et al.19 These researchers conducted a randomized, double-blind, placebo-controlled study over three days to assess the effects of a commercial, cold-water-dispersible curcumin, HydroCurc, on exercise recovery when consumed as a drink by recreationally trained, healthy males. The study included 28 healthy males with strength-training experience. Participants received a single dose of 1000 mg of powder containing 500 mg of HydroCurc, which contains 427 mg of curcuminoids, or a matched placebo drink. The supplement was dispersed in 250 ml of water, pre-exercise and at 24 hours and 48 hours postexercise.

Pain was evaluated using a visual analog scale (VAS), as was thigh circumference (TC), lactate, creatine kinase (CK), LDH, high-sensitivity C-reactive protein (HS-CRP), myoglobin (Mb), IL-6, IL-10, and TNF-α levels. At 48-h and 72-h postexercise, higher muscle pain was reported in the placebo group than in the curcumin group, which suggests that the curcumin treatment might provide a quicker return to exercise training than the placebo, by reducing postexercise pain, modulating inflammatory pathways, and reducing lactate accumulation.

The IL-6 levels were significantly higher at one hour (P < .05), 24 h (P < .01), and 72 h (P < .05) postexercise in the curcumin group than in the placebo group. No significant differences were observed between the groups for CK, LDH, Mb, HS-CRP, or TNF-α levels at any time point.

Thanawala et al.20 These researchers conducted a randomized, double-blind, placebo-controlled, parallel-group study to evaluate the efficacy, safety, and tolerability of a commercial supplement, a Natural, Water-Dispersible Turmeric Extract (WDTE60N) TurnXTRA 60N, on DOMS in comparison with a placebo for 30 recreationally active, healthy participants. Participants were randomly assigned to receive a 250-mg capsule, containing 150 mg of curcuminoids or a placebo, once daily for 33 days, with a pre-exercise period of 29 days and a postexercise period of 4 days.

Pain intensity was assessed using a VAS scale and measured before and immediately after exercise and at 12, 24, 48, 72, and 96 h after eccentric exercise. Participants’ well-being was assessed using the adapted version of the Hooper and MacKinnon questionnaire at the same time points. The muscle-damage markers serum CK and serum LDH were measured at baseline and at 24, 48, 72, and 96 h after eccentric exercise.

The turmeric extract group reported significantly less pain after eccentric exercise compared to the placebo group, based on the VAS score at the 12-hour time point. For all of the adapted Hooper and MacKinnon questionnaire’s subdomains—fatigue, mood, general muscle soreness, sleep quality, and stress, the turmeric extract group demonstrated significantly greater improvement postexercise including overall well-being, compared to the placebo group.

A decrease in serum CK levels and significantly lower serum LDH levels were also observed in the turmeric extract group compared to the placebo group. The study showed that an intake of a water dispersible turmeric extract before and after eccentric exercise could significantly reduce subjective perceptions of pain and muscle soreness as well as serum LDH activity, and the extract also significantly improved sleep quality and psychological well-being in recreationally active participants compared to placebo.

Jäger et al.22 These researchers conducted a randomized, double-blind, placebo-controlled study to examine the effects...
of a commercial curcumin supplement, CurcuWIN. The study examined the effects of a low dose of 250 mg test product, containing 50 mg curcuminoids, and of a high dose of 1000 mg test product, containing 200 mg of curcuminoids, on blood flow, exercise performance, and muscle damage in physically active individuals.

The 63 eligible participants, divided into 3 groups, were randomly assigned to ingest a low dose or a high dose of the supplement or a placebo daily for 8 weeks. Muscle function, as measured using isokinetic dynamometry, and perceived soreness were assessed at baseline and at one, 24, 48, and 72 hours after a downhill run. Nonsignificant improvements in total soreness were observed in the 1000-mg group. When compared to the placebo group, that group showed attenuated reductions for some, but not all, outcome measures for performance and soreness after completion of a downhill running bout. Additionally, the 250-mg dose didn't offer any advantage over the placebo group.

**Table 1. Safety and Efficacy of Monotherapy With Turmeric Extracts and Curcumin Supplements in Exercise-related Skeletal-muscle Health. None of the studies reported an adverse event.**

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Age, y</th>
<th>Treatment</th>
<th>Curcuminoids/ Curcumin Administered Daily</th>
<th>Indication</th>
<th>Duration</th>
<th>Scale</th>
<th>Mean ± SD</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mallard et al, 2020&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Intervention group (n=21)</td>
<td>18-29</td>
<td>LD: 250 mg daily of curcumin; HD: 1000 mg daily of curcumin</td>
<td>LD: 50 mg curcuminoids HD: 200 mg of curcuminoids</td>
<td>Muscle-damaging exercise</td>
<td>56 days</td>
<td>VAS</td>
<td>2.70 ± 0.46</td>
<td>• In intervention group, lower pain was evident within 12 hours of eccentric exercise, thus indicating faster recovery. • Significantly reduced muscle soreness postintervention</td>
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<td></td>
<td>Placebo group (n=20)</td>
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<td>Thanawala et al, 2022&lt;sup&gt;24&lt;/sup&gt;</td>
<td>Intervention group (n=15)</td>
<td>18-35</td>
<td>250 mg of natural, water-dispersable turmeric extract in capsule, once daily</td>
<td>150 mg curcuminoids</td>
<td>DOMS</td>
<td>33 days</td>
<td>VAS (hrs)</td>
<td>Intervention: 12, 24, 48, 72, 96, Placebo: 12, 24, 48, 72, 96</td>
<td>• In intervention group, lower pain was evident within 12 hours of eccentric exercise, thus indicating faster recovery. • Significantly reduced muscle soreness postintervention</td>
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<td></td>
<td>Placebo group (n=15)</td>
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<td>Jager et al, 2019&lt;sup&gt;23&lt;/sup&gt;</td>
<td>Intervention LD group (n=20)</td>
<td>19-29</td>
<td>90 mg twice daily of surface-controlled water-dispersible curcumin, for 180 mg/day</td>
<td>64.8 mg of curcuminoids</td>
<td>Exercise-induced muscle soreness</td>
<td>4 days</td>
<td>VAS</td>
<td>1.17 ± 0.52</td>
<td>• In 50-mg curcuminoids group, observed decreases in peak extension torque values occurred at one and 24 h after muscle-damaging exercise. • In 200-mg curcuminoids group, attenuated reductions occurred in some but not all participants.</td>
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<td></td>
<td>Intervention HD group (n=22)</td>
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<td></td>
<td>Placebo group (n=21)</td>
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<td>Tanabe et al, 2019&lt;sup&gt;20&lt;/sup&gt;</td>
<td>Intervention PRE group (n=8)</td>
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<td>500 mg once daily of turmeric matrix formulated in a capsule</td>
<td>250 mg of curcuminoids</td>
<td>DOMS, induced by eccentric continuous exercise</td>
<td>4 days</td>
<td>VAS</td>
<td>2.90 ± 0.39</td>
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<td>Test POST group (n=8)</td>
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<td>Placebo group (n=8)</td>
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<tr>
<td>Amidzé et al, 2020&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Intervention group (n=15)</td>
<td>21 (avg age)</td>
<td>1000 mg of curcumin-phosphatidylcholine complex twice daily, for 2000 mg/day</td>
<td>400 mg of curcumin</td>
<td>DOMS</td>
<td>4 days</td>
<td>Pain intensity point scale (0-4)</td>
<td>Intervention: 23.3 ± 7.9 (17.2, 29.4) Placebo: 30.6 ± 7.9 (24.8, 36.2)</td>
<td>• After 4 days, curcumin was effective in preventing DOMS by reducing pain intensity and muscle injury.</td>
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<td></td>
<td>Placebo group (n=15)</td>
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<td>Drbovic et al, 2014&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Intervention group (n=9)</td>
<td></td>
<td></td>
<td>1500 mg daily of NCE extract</td>
<td>230.9 mg of curcumin</td>
<td>Injury risk on drop jumps</td>
<td>28 days</td>
<td>No pain assessment endpoint</td>
<td>• After 28 days of supplementation, NCE was effective, providing a variety of benefits for athletes.</td>
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<td></td>
<td>Placebo group (n=10)</td>
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Abbreviations: DOMS, delayed-onset muscle soreness; HD, high dose; LD, low dose; NCE, Nanobubbles water curcumin extract; VAS, Visual analogue scale.
The 24 participants were randomly assigned to one of three groups. The two intervention groups received 90 mg twice daily, or 180 mg/d, of the test product, containing 32.4 mg curcuminoids: (1) the PRE group, for 7 days before exercise, and (2) the POST group, for 4 days after exercise. The CON group received a placebo for 4 days after exercise.

The maximal voluntary contraction (MVC) torque of the elbow flexors, elbow joint range of motion (ROM), muscle soreness, and serum creatine kinase (CK) activity were measured at baseline, immediately after, and at 1, 2, 3, and 4 days after exercise. In the POST group, ROM was higher at 3-4 days and muscle soreness was lower at 3 days after exercise than in the CON group (P<.05). However, in the PRE group, no significant differences existed in ROM and muscle soreness compared to those in the CON group after exercise. Additionally, no significant differences existed between the groups in terms of changes in MVC torque or serum CK activity.

Amalraj et al.24 These researchers conducted a randomized, placebo-controlled, double-blind clinical study to test the efficacy of a commercial, complete natural turmeric matrix formulation, Cureit, in decreasing damage from oxidative stress and inflammation related to severe muscle damage induced by eccentric continuous exercise. The 30 participants were randomly assigned to one of two treatment groups and took either a 500 mg capsule of the test product, containing 250 mg of curcuminoids, or a placebo for 4 days.

Pain reduction was assessed using a VAS. No significant reduction in the VAS scores for pain occurred between baseline and postintervention for the participants treated with curcumin, and no significant differences were observed in the placebo group. The oral consumption of curcumin significantly reduced DOMS and caused a nonsignificant reduction in CK concentrations and a slight increase in the VO2 max value as compared with the placebo.

Drobnic et al.10 These researchers performed a randomized, placebo-controlled, single-blinded, pilot study to examine whether a commercial, curcumin-phosphatidylcholine complex, Meriva, could attenuate damage from oxidative stress and inflammation related to acute muscle injury induced by eccentric continuous exercise. The 20 male participants were randomly assigned to receive either 1000 mg of the test product, containing 200 mg of curcumin, or a matching placebo, both twice daily.

Supplementation was initiated at 48 h prior to the test and continued for 24 h after exercise. Muscle damage was quantified by magnetic resonance imaging (MRI), laboratory tests, and histological analyses of muscle samples obtained at 48 h after the exercise. Pain intensity was recorded using a pain-intensity scale (0-4). Participants in the curcumin group reported less pain in the lower limbs than those in the placebo group, and the results were significant only for the right and left anterior thighs out of the three compartments evaluated—anterior, posterior, and medial.

Significantly fewer participants in the curcumin group had MRI evidence of muscle injury in the posterior or medial compartments of either thigh. No significant differences existed in the levels of the muscle-damage markers CK, HS-CRP, and monocyte chemoattractant protein-1 (MCP-1) in either group postintervention, except IL-8, which was significantly lower in the curcumin group only at 2 h after exercise. No differences in oxidative stress markers or muscle histology were observed.

Wang et al.25 These researchers conducted a study to evaluate the effects of nanobubbles water curcumin extract (NCE) on reducing the risk of musculoskeletal injury in 12 female participants. Participants were randomly assigned to receive either 1500 mg of NCE, containing 230.9 mg curcumin, or a placebo daily for 4 weeks. Postintervention, the muscle-strength indices, contact time, significantly increased for the 100% drop jumps.

The levels of the muscle-damage marker CK weren't significantly different between the placebo and NCE groups. Postintervention, the NCE supplementation had decreased the peak vertical ground reaction force (PVGRF) during drop jumps, which might help reduce the risk of injury for drop jumps.

Muscle Health: Meta-analysis

For participants aged 18-35 years, who were treated with monotherapy using turmeric extracts and curcumin supplements, pain intensity was assessed using a VAS or a pain intensity point scale. Curcumin was effective and well-tolerated in reducing pain intensity. The water dispersible turmeric extract demonstrated significant reductions in pain intensity within 12 h postexercise, compared to other turmeric extract and curcumin supplements. Thus, the water dispersible turmeric extract proved to be more effective and safer than other turmeric extracts and curcumin supplements for the management of exercise-related skeletal muscle health.

Statistical Analysis

The research team analyzed the data in the meta-analysis using NCSS 2021 statistical software (Utah, USA). The Odds Ratio (OR) or Mean Difference (MD) and the 95% Confidence Intervals (CIs) were used as the efficacy and safety statistics. The Chi-square (χ²) test was used to evaluate the heterogeneity in the literature. If the studies weren't heterogeneous, they were analyzed using a fixed-effects model; if they were heterogeneous, a random-effects model was used.

Two RCTs that studied DOMS and that used supplements that were either a water dispersible turmeric extract or a turmeric matrix formulation, had used VAS to evaluate pain as an efficacy parameter and were included in the analysis.

Results

The heterogeneity analysis found an χ² value for Cochran's Q statistic of 29.3765 and P<.0001, which showed that statistical heterogeneity existed between the two studies; therefore, the random effects model was used. The χ² value of the random effects model was 216.5545 with P<.0001, which was statistically significant. Table 2 shows that the difference between the intervention and control groups was significant for both muscle damage markers CK and HS-CRP.
### Table 2. Efficacy of Turmeric Extracts and Curcumin Supplements in Exercise-related Skeletal Muscles Health Using Random Effect Model

<table>
<thead>
<tr>
<th>Product Comparison</th>
<th>Mean Difference</th>
<th>Standard Error</th>
<th>95% CI</th>
<th>Weightage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention vs Comparator</td>
<td>-1.2</td>
<td>0.18</td>
<td>[-1.57, -0.83]</td>
<td>50.00</td>
</tr>
<tr>
<td>Thanaewala et al&lt;sup&gt;27&lt;/sup&gt;: water dispersible turmeric extract and placebo</td>
<td>-2.6</td>
<td>0.18</td>
<td>[-2.97, -2.23]</td>
<td>50.00</td>
</tr>
<tr>
<td>Combined</td>
<td>-1.9</td>
<td>0.7</td>
<td>[-3.27, -0.53]</td>
<td></td>
</tr>
<tr>
<td>New vs existing treatment: water dispersible turmeric extract vs turmeric matrix formulation</td>
<td>-0.47</td>
<td>0.19</td>
<td>[-0.85, -0.09]</td>
<td></td>
</tr>
</tbody>
</table>

In addition, when comparing the efficacy between the water dispersible turmeric extract and the turmeric matrix formulation using VAS for pain as an efficacy parameter, the meta-analysis showed a statistically significant difference between the two groups [SMD -0.47 (-0.85; -0.09), P<.0116].

The differences between the water dispersible turmeric extract and the placebo and between the turmeric matrix formulation and the placebo were statistically significant, with [SMD -1.2 (-1.5743, -0.8252), P<.00001] and [SMD -2.6 (-2.974, -2.226), P<.00001], respectively.

The forest plot shows the results of each study in a single plot (Figure 2). The size of the plot symbols is proportional to the sample size of the study. The points on the plot are sorted by study and mean difference. The lines represent the confidence intervals for the mean differences. A narrow confidence interval indicates a greater degree of precision.

### Joint Health: Systematic Review

The most common joint health disorders include chronic knee pain, knee OA, and RA. The effects of curcumin on joint health and these disorders have been evaluated in several clinical trials pertaining to its potent anti-inflammatory action. Tables 3 and 4 show the characteristics of the included studies.

**Thanawala et al.**<sup>26</sup> These researchers conducted a double-blind, randomized, placebo-controlled, parallel-group study of healthy participants with chronic knee pain.

### Table 3. Safety and Efficacy of Monotherapy With Turmeric Extracts and Curcumin Supplements for Joint Health, Using VAS Scale

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Age, y</th>
<th>Treatment</th>
<th>Curcuminoids / Curcumin Administered Daily</th>
<th>Indication</th>
<th>Duration</th>
<th>Scale</th>
<th>Mean ± SD</th>
<th>AE/ safety</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thanaewala et al, 2021&lt;sup&gt;27&lt;/sup&gt;</td>
<td>Intervention group (n=53)</td>
<td>18-60</td>
<td>250 mg once daily of water dispersible turmeric extract in capsule</td>
<td>150 mg of curcuminoids</td>
<td>Chronic knee pain</td>
<td>90 days</td>
<td>VAS Baseline to day 90</td>
<td>Intervention Baseline: 5.4 ± 0.9</td>
<td>Placebo Baseline: -1.5 ± 0.7</td>
<td>Restlessness (4.11%), tingling sensation (1.37%)</td>
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<td></td>
<td>Placebo group (n=53)</td>
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<td></td>
<td>Day 90: 5.8 ± 0.8</td>
<td>Day 90: -0.6 ± 0.8</td>
<td>No AEs reported</td>
</tr>
<tr>
<td>Singh et al, 2021&lt;sup&gt;28&lt;/sup&gt;</td>
<td>Intervention group (n=73)</td>
<td>40-80</td>
<td>500 mg twice daily of curcuminoid-essential oil complex in capsule, for 1000 mg/ day</td>
<td>950 mg of curcuminoids</td>
<td>Knee OA</td>
<td>42 days</td>
<td>WOMAC Baseline to Week 6</td>
<td>Intervention Baseline: 56.3 (20.5)</td>
<td>Paracetamol Baseline: 50.2 (19.5)</td>
<td>Mild nausea and diarrhea</td>
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<td></td>
<td>Paracetamol group (n=71)</td>
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<td></td>
<td>Week 6: 43.01 ± 2.62</td>
<td>Week 6: 37.93 ± 2.16</td>
<td>After 42 days, bioavailable turmeric extract was effective in reducing pain and other symptoms of knee OA and found to be safe.</td>
</tr>
<tr>
<td>Amalraj et al, 2017&lt;sup&gt;29&lt;/sup&gt;</td>
<td>Intervention: LD group: (n=12)</td>
<td></td>
<td>LD turmeric matrix capsule, 250 mg twice daily, 500 mg/ day</td>
<td>LD: 250 mg curcuminoids</td>
<td>RA</td>
<td>90 days</td>
<td>VAS and DAS28</td>
<td>VAS Intervention LD Baseline: 7.01 ± 0.86</td>
<td>Postintervention: 2.63 ± 0.74</td>
<td>After 90 days, turmeric matrix formula acted as an analgesic, anti-inflammatory agent for the management of RA and was well tolerated and without side effects.</td>
</tr>
<tr>
<td></td>
<td>HD group: (n=12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Intervention HD Baseline: 7.99 ± 0.71</td>
<td>Postintervention: 2.21 ± 0.45</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Placebo group (n=12)</td>
<td></td>
<td></td>
<td>HD turmeric matrix capsule, 500 mg twice daily, 1000 mg/ day</td>
<td>Placebo</td>
<td></td>
<td></td>
<td>Placebo Baseline: 8.61 ± 0.73</td>
<td>Postintervention: 6.84 ± 0.63</td>
<td></td>
</tr>
</tbody>
</table>

*AE* = adverse event; *VAS* = visual analog scale; *RA* = rheumatoid arthritis; *OA* = osteoarthritis; *HD* = high dose; *LD* = low dose.
Table 3. (continued)

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Age, y</th>
<th>Treatment</th>
<th>Curcuminoids / Curcumin Administered Daily</th>
<th>Indication</th>
<th>Duration</th>
<th>Scale</th>
<th>Mean ± SD</th>
<th>AE/ safety</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kuptniratsaikul et al, 2009*</td>
<td>Intervention group (n=52)</td>
<td>50</td>
<td>500 mg of Curcuma domestica four times daily, 2000 mg/day</td>
<td>1000 mg of curcuminoids</td>
<td>Knee OA</td>
<td>42 days</td>
<td>Numeric scale</td>
<td>Week 0 to Week 6</td>
<td>Intervention Pain on level walking.</td>
<td>Dysepsia (20.8%), dizziness (10.4%), nausea/ vomiting (6.3%), and loose stool (4.2%).</td>
</tr>
<tr>
<td></td>
<td>Placebo group (n=55)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atabaki et al, 2020*</td>
<td>32</td>
<td>Placebo (n=38)</td>
<td>Intervention LD group (n=48)</td>
<td>Knee OA</td>
<td>90 days</td>
<td>VAS</td>
<td>Predose, postdose</td>
<td>VAS Intervention Predose: 7.93 ± 0.39</td>
<td>No AEs reported</td>
</tr>
<tr>
<td></td>
<td>Henrotin et al, 2019*</td>
<td>25</td>
<td>Placebo (n=24)</td>
<td>Intervention LD group (n=38)</td>
<td>Knee OA</td>
<td>90 days</td>
<td>VAS</td>
<td>KOOS Baseline to Postintervention</td>
<td>VAS Intervention Baseline 53.2 ± 5.70</td>
<td>No AEs reported</td>
</tr>
<tr>
<td></td>
<td>Placebo group (n=35)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Javadi et al, 31</td>
<td>35</td>
<td>Placebo (n=15)</td>
<td>Intervention LD group (n=25)</td>
<td>Knee OA</td>
<td>38 days</td>
<td>VAS</td>
<td>Predose, postdose</td>
<td>VAS Intervention Predose: 6.1 ± 0.30</td>
<td>No AEs reported</td>
</tr>
<tr>
<td></td>
<td>Placebo group (n=24)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Henrotin et al, 2019*</td>
<td>38</td>
<td>Placebo (n=25)</td>
<td>Intervention LD group (n=38)</td>
<td>Knee OA</td>
<td>90 days</td>
<td>VAS</td>
<td>KOOS HD and LD</td>
<td>VAS Baseline Intervention HD 62.9 ± 13.8</td>
<td>No severe AEs</td>
</tr>
<tr>
<td></td>
<td>Placebo (n=40)</td>
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<td></td>
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<td></td>
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</tr>
</tbody>
</table>

* Placebo (n=40) 

** Placebo (n=35) 

*** Placebo (n=40)
Using VAS Scale

WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Abbreviations:

Table 4

Safety and Efficacy of Combination Therapy With Turmeric Extracts and Curcumin Supplements for Joint Health Using VAS Scale

Abbreviations:

following physical exertion. The 106 participants were randomly assigned to two groups: group 1 was administered 250 mg of a commercial, water dispersible turmeric extract, TurmXTRA 60N, in one capsule containing 150 mg curcuminoids, and group 2 received a placebo, both once daily for 90 days.

Reduction in pain intensity was measured using a VAS after an 80-m, fast-paced walk test. The turmeric extract significantly reduced the VAS score between baseline and day 90, with a greater mean reduction, 2.5 times, than that for the placebo. It also significantly decreased time taken for the 80-m, fast-paced walk test and nine-step stair-climb test, and improved all inflammatory biomarkers compared to the placebo, with a significant reduction in median TNF-α and MMP-3 compared to baseline. The study showed that the water dispersible turmeric extract significantly alleviated knee pain and improved joint function in healthy participants with chronic knee pain.

Singhal et al. These researchers conducted a study to compare the efficacy and safety of a commercial, curcuminoid-essential oil complex BCM-95, Curcugreen, and paracetamol in 144 patients with knee OA. One group received 500 mg of the oil complex, containing 475 mg curcuminoids, twice daily, and the other group received 650 mg of paracetamol three times daily, for 6 weeks.

The intensity of pain and other symptoms of OA were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale. After 6 weeks of treatment, most patients in the curcumin group reported improvement in WOMAC pain and function and stiffness scores. The C-reactive protein (CRP) and TNF-α levels were significantly reduced in the curcumin group.
Amalraj et al. These researchers conducted a three-arm study to compare the efficacy of two doses of a commercial, complete natural turmeric matrix formulation, Acumin, with that of a placebo for patients with active RA. The 36 participants were randomly assigned to one of three groups. Twice daily for 90 days, participants received either a placebo or a low, 250-mg dose of the matrix formulation containing 125 mg of curcuminoids, or a high, 500 mg dose of the matrix formulation containing 250 mg of curcuminoids.

Participants’ responses were assessed using the American College of Rheumatology (ACR) criteria response,30 a V AS, the Disease Activity Score 28 (DAS28),31 and CRP levels. Both matrix formulations demonstrated significant anti-inflammatory and analgesic properties by improving the erythrocyte sedimentation rate (ESR), CRP, V AS, rheumatoid factor (RF), DAS28, and ACR responses relative to the baseline. The high dose curcumin group showed greater reductions in the DAS and V AS scores.

Kuptniratsaikul et al.32 These researchers conducted an RCT to determine the efficacy and safety of Curcuma domestica (C. Domestica) extracts for pain reduction and functional improvement in patients with knee OA. The 107 patients with primary knee OA who had pain scores of greater than or equal to 5 of 10 on a numerical rating scale were randomly divided into two groups. They received either 500 mg of the C. Domestica extract, containing 250 mg of curcuminoids, four times daily, or 800 mg of ibuprofen daily for 6 weeks.

Pain intensity was assessed using a numerical rating scale, and knee function was assessed by the time spent on a 100-m walk and going up and down a flight of stairs with 10 steps. All parameters showed decreasing trends in both groups. No significant difference existed in the scores among patients receiving ibuprofen or C. domestica.

Javadi et al.33 These researchers conducted a randomized, double-blind, controlled study to determine the effects of commercial curcumin nanomicelles, SinaCurcumin, on the clinical symptoms of patients with RA. The 65 patients were divided into two groups, with one to receive 40 mg of curcumin nanomicelles in a capsule and the other a placebo capsule, both three times daily for 12 weeks.

Disease activity was measured using the DAS28 after 12 weeks, which showed a reduction in both groups. However, the difference between the two groups wasn’t significant.

Atabaki et al.34 These researchers conducted a double-blind, randomized, placebo-controlled study to assess the effects of commercial curcumin nanomicelles, SinaCurcumin, on the immune responses of patients with OA. The 30 patients were equally divided into two groups: one group received 80 mg of curcumin nanomicelles, and the other group received a placebo, both once a day for 3 months. In addition, all participants received 50 mg of diclofenac sodium.

The intervention group had decreased scores on a V AS; decreased levels of CRP, CD4+, CD8+ T cells, and Th17 cells; and decreased B-cell frequency, demonstrating a significant reduction in inflammation and pain in patients with OA.

Shep et al.35 These researchers conducted a randomized, open-label, parallel, active-controlled study in patients with knee OA to compare the efficacy and safety of a commercial, curcuminoid-essential oil complex, BCM-95, with that of diclofenac. The study included 139 patients who were randomly assigned to receive either 500 mg of the oil complex, containing 475 mg curcuminoids, in a capsule three times daily or a 50-mg tablet of diclofenac twice daily for 28 days.

Pain was evaluated using the VAS and the Knee Injury and Osteoarthritis Outcome Score (KOOS).36 Patients who received curcumin showed a improvement in the KOOS score and pain severity that was similar to that of diclofenac.

Henrotin et al.37 These researchers conducted a randomized, double-blind, placebo-controlled study to compare the efficacy of two doses of a commercial, bio-optimized Curcuma longa extract (BCL), Flexofytol, which contains 46.67 mg of turmeric rhizome extract, for symptomatic knee OA. 150 patients with knee OA in the study were followed up for 90 days. Patients were randomly assigned to one of three groups, receiving either three placebo capsules twice a day, a low dose of curcumin in two capsules plus one capsule of placebo twice a day, or a high dose of curcumin in 3 capsules twice a day.

Pain intensity was assessed using VAS and KOOS Scores. Pain reduction at day 90 in the low- and high-dose BCL groups, at -29.5 mm and -36.5 mm, respectively, was higher than that in the placebo group. The KOOS global score and subscales were significantly improved over time in all the groups (P<.001), and no significant differences existed between the groups. Significantly more AEs occurred in the high-dose curcumin group than in the low-dose curcumin and placebo groups.

Gupte et al.38 These researchers performed a randomized, placebo-controlled study to evaluate the efficacy and safety of commercial, solid lipid curcumin particles (SLCP), Longvida, in 42 patients with knee OA. The patients were randomly assigned to receive 400 mg in an SLCP capsule containing 80 mg of curcumin twice daily or 400 mg of ibuprofen in a placebo capsule once daily, for 90 days.

Knee pain and function were assessed using WOMAC and a VAS. Curcumin significantly decreased the VAS and WOMAC scores compared to baseline from day 45 onward. This effect was comparable to that of the low-dose ibuprofen used in the study.

Nakagawa et al.39 These researchers performed an open-label, noncomparative study to evaluate the efficacy and safety of a commercial, surface-controlled water-dispersible curcumin, Theracurmin, in knee OA. The 50 patients were randomly assigned to receive 90 mg of curcumin, containing 32.4 mg curcuminoids, or a placebo, both twice daily in 6 capsules daily for 6 months.

Knee symptoms were measured using the Japanese Knee Osteoarthritis Measure (JKOM) and the knee scoring system of the Japanese Orthopedic Association (JOA). A knee pain VAS is included in the JKOM. The VAS, JKOM, and JOA scores at 6 months after treatment were significantly better than those at baseline.
Belcaro et al. These researchers conducted a three-month pilot study to assess the efficacy and safety of a commercial curcumin-phosphatidylcholine complex, Meriva, in 50 patients with OA. Participants in Group A were assigned to receive either the best available treatment as defined by a patient's physician; and Group B was managed using the best available treatment plus 1000 mg of a curcumin-phosphatidylcholine complex containing 200 mg curcumin, daily for 3 months.

The WOMAC score was used to assess pain intensity. At the end of treatment, the reduction in the WOMAC score in the curcumin group was significantly greater than that in the control group.

Panahi et al. These researchers conducted a randomized, double-blind, placebo-controlled study to investigate the efficacy of a curcuminoid-piperine supplement, C3 Curcumin Complex, in reducing the systemic oxidative burden in patients with knee OA. The 40 patients with mild-to-moderate, primary knee OA were randomly divided into two groups, with one group receiving 500 mg of curcuminoids plus 5 mg of piperine (Bioperine) in a capsule three times daily or matched placebo capsules, for 6 weeks.

A significant improvement was observed in the systemic oxidative stress biomarkers after 6 weeks of curcuminoid-piperine supplementation. A significant elevation in serum superoxide dismutase (SOD) activity and in glutathione (GSH) concentrations occurred as well as a significant reduction in malondialdehyde (MDA) concentrations in the curcuminoid-piperine group compared to the placebo group.

Rahimnia et al. These researchers performed a three-group study to determine effects of a curcuminoid-piperine formulation on inflammatory biomarkers in 40 patients with OA. Patients were randomly allocated to receive either 500 mg of curcuminoids plus 5 mg of piperine (Bioperine) in a capsule or a placebo, three times daily for 6 weeks.

Serum levels of inflammatory biomarkers, such as IL-4, IL-6, TNF-α, transforming growth factor-β (TGF-β), and HS-CRP, together with ESR, were determined at baseline and at the end of the trial. A comparison of the magnitude of the changes in the evaluated inflammatory biomarkers indicated no significant differences between the groups.

Joint Health: Meta-analysis

Participants aged 18 to 80 years were treated with either a monotherapy, a turmeric extract standardized for curcuminoids, or a combination of a curcuminoids and a pharmaceutical treatment. Pain intensity was assessed usingVAS, WOMAC, DAS28, JCOM, JOA, KOOS, a numerical rating scale, and ACR, and Lequesne’s Pain Functional Index (LPFI). The studies for both monotherapy and the combination therapies concluded that curcumin was effective in reducing pain intensity and improving joint function, with no major or severe AEs.

Table 5. Efficacy of Turmeric Extracts and Curcumin Supplements in Joint Health Using Random Effects Model

<table>
<thead>
<tr>
<th>Product Comparison</th>
<th>Mean Difference</th>
<th>Standard Error</th>
<th>95% CI</th>
<th>Weightage %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention vs Comparator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amalraj et al.</td>
<td>-4.21</td>
<td>0.28</td>
<td>[-4.79, -3.63]</td>
<td>17.33</td>
</tr>
<tr>
<td>High-dose curcumin matrix formulation and placebo</td>
<td>-4.63</td>
<td>0.22</td>
<td>[-5.09, -4.17]</td>
<td>17.36</td>
</tr>
<tr>
<td>Average</td>
<td>0</td>
<td>0</td>
<td>[-4.86, -4.05]</td>
<td>17.33</td>
</tr>
<tr>
<td>Shep et al.</td>
<td>0</td>
<td>0.12</td>
<td>[-0.24, 0.24]</td>
<td>17.39</td>
</tr>
<tr>
<td>C3 Complex</td>
<td>0</td>
<td>0.10</td>
<td>[-0.89, -0.51]</td>
<td>17.39</td>
</tr>
<tr>
<td>Average</td>
<td>0</td>
<td>0</td>
<td>[-0.89, -0.51]</td>
<td>17.39</td>
</tr>
</tbody>
</table>

Results

The heterogeneity analysis found a $\chi^2$ value for Cochran’s Q statistic of 3666.80 and $P<.0001$, which showed that statistical heterogeneity existed among the studies; therefore, the random effects model was used. The $\chi^2$ value of the random effects model was 1400.65, with $P<.0001$, which was statistically significant. Table 5 shows that the difference between the intervention and control groups was statistically significant [SMD 0.12 (-3.59; 3.85), $P<.0001$].

The research team analyzed data for five RCTs for patients with RA, OA, chronic knee pain, or knee OA. The studies used treatments: (1) a low dose of turmeric matrix formulation, (2) a high dose of a turmeric matrix formulation, (3) a curcuminoid essential oil complex, (4) curcumin nanomicelles, (5) a water dispersible turmeric extract, (6) a high dose of bio-optimized Curcuma longa extract, and (7) a low dose of bio-optimized Curcuma longa extract. The VAS score was considered to be an efficacy parameter.

Significant differences existed between groups: (1) between the low-dose turmeric matrix formulation and the placebo [SMD -4.21 (-4.79, -3.63)], (2) between the high-dose turmeric matrix formulation and the placebo [SMD -4.63 (-5.09, -4.17), (1) & (2) combined $P < .00001$], (3) between the curcumin nanomicelles and the placebo [SMD -5.70 (-5.89, -5.51), $P < .00001$], (4) between the water dispersible turmeric extract and the placebo [SMD 4.40 (4.09, 4.71), $P < .00001$], (5) between the high-dose bio-optimized Curcuma longa extract and the placebo [SMD 13.15 (2.36, 23.94)], and (6) between the low-dose bio-optimized Curcuma longa extract and the placebo with [SMD 15.75 (3.23, 28.27), (5) & (6) combined $P < .00001$].
Figure 3 shows the forest plot for each study on a single plot. The size of the plot symbols is proportional to the sample size of the study. The points on the plot are sorted by study and mean difference. The lines represent the confidence intervals for the mean differences. A narrow confidence interval indicates a greater degree of precision.

The heterogeneity analysis had a χ² value for Cochran's Q statistic of 372.6017, with P < .0001, which showed that statistical heterogeneity existed among the studies; therefore, the random effects model was used. The χ² value of the random effects existed among the studies; therefore, the random effects model was used. The χ² value of the random effects model was 48.0968 (P < .0001), which was statistically significant. Table 6 shows that the difference between the intervention and control groups was statistically significant [SMD -0.76 (-1.86, 0.337], P < .00001].

Statistically significant differences existed between groups: (1) between the water dispersible turmeric extract and the low-dose bio-optimized Curcuma longa extract [SMD -24.20 (-31.87, -16.53), (2) between the curcuminoid-essential oil complex and the high-dose bio-optimized Curcuma longa extract [SMD -23.20 (-29.58, -16.82), and (3) between the water dispersible turmeric extract and the high-dose bio-optimized Curcuma longa extract [SMD -21.60 (-28.95, -14.25).

Figure 4 shows a forest plot that presents the results of each study on a single plot. It shows that the studies with no significant differences tentatively fell on the plot's vertical line. Those comparisons were: (1) the water dispersible turmeric extract and the curcuminoid-essential oil complex [SMD 1.60 (1.31, 1.89)], (2) between the curcumin nanomicelles and the curcuminoid-essential oil complex [SMD 1.20 (0.78, 1.62)], (3) between the water dispersible turmeric extract and the low-dose turmeric matrix formulation [SMD 1.17 (0.67, 1.67)], and (4) between the high-dose turmeric matrix formulation and the curcumin nanomicelles [SMD -1.19 (-1.48, -0.90)].

On Figure 4, the size of the plot symbols is proportional to the sample size of the study. The points on the plot are sorted by study and mean difference. The lines represent the confidence intervals for the mean differences. A narrow confidence interval indicates a greater degree of precision.

**Table 6. Efficacy of Curcumin Supplements Using Random Effects Model.**

<table>
<thead>
<tr>
<th>Product Comparison</th>
<th>Mean Difference</th>
<th>Standard Error</th>
<th>95% CI</th>
<th>Weightage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention vs Comparator</td>
<td>-24.20</td>
<td>3.8547</td>
<td>[-31.87, -16.53]</td>
<td>1.8195</td>
</tr>
<tr>
<td>Curcuminoid-essential oil complex and high-dose Curcuma longa extract</td>
<td>-23.20</td>
<td>3.3731</td>
<td>[-29.58, -16.82]</td>
<td>2.4628</td>
</tr>
<tr>
<td>Curcuma longa extract</td>
<td>-21.60</td>
<td>3.7065</td>
<td>[-28.95, -14.25]</td>
<td>1.9466</td>
</tr>
<tr>
<td>Water dispersible turmeric extract and curcumin nanomicelles</td>
<td>-1.19</td>
<td>0.1396</td>
<td>[-1.48, -0.90]</td>
<td>13.4372</td>
</tr>
<tr>
<td>Water dispersible turmeric extract and curcuminoid-essential oil complex</td>
<td>0.40</td>
<td>0.2108</td>
<td>[-0.02, 0.82]</td>
<td>13.2944</td>
</tr>
<tr>
<td>Low Dose and high dose turmeric matrix formulation and curcumin nanomicelles</td>
<td>0.42</td>
<td>0.2500</td>
<td>[-0.10, 0.94]</td>
<td>13.1929</td>
</tr>
<tr>
<td>Curcumin nanomicelles and curcuminoid-essential oil complex</td>
<td>1.37</td>
<td>0.2525</td>
<td>[0.67, 1.67]</td>
<td>13.1860</td>
</tr>
<tr>
<td>Water dispersible turmeric extract and low-dose turmeric matrix formulation</td>
<td>1.20</td>
<td>0.2125</td>
<td>[0.78, 1.62]</td>
<td>13.2904</td>
</tr>
<tr>
<td>Water dispersible turmeric extract and high-dose turmeric matrix formulation</td>
<td>1.59</td>
<td>0.2400</td>
<td>[1.11, 2.07]</td>
<td>13.2204</td>
</tr>
<tr>
<td>Combined</td>
<td>1.60</td>
<td>0.1467</td>
<td>[1.31, 1.89]</td>
<td>13.4254</td>
</tr>
<tr>
<td>Average</td>
<td>-0.76</td>
<td>0.5588</td>
<td>[-1.86, 0.337]</td>
<td>13.4254</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The current meta-analysis has demonstrated the effectiveness of curcumin in skeletal muscle health. Several studies in the current review demonstrated that turmeric extract and curcumin can effectively reduce postexercise pain, inflammation, oxidative stress, and muscle soreness. Thanawala et al26 conducted a study and reported that the intake of 250 mg of water dispersible turmeric extract before...
and after eccentric exercise could significantly reduce the subjective perception of muscle soreness. 

Mallard et al,18 Jager et al,22 Drobnic et al,19 Tanabe et al,23 and Amalraj et al24 demonstrated the effectiveness of curcumin in reducing postexercise pain, modulating inflammatory pathways, reducing lactate accumulation in an exercising population, attenuating damage from oxidative stress and inflammation related to acute muscle injury, and reducing DOMS without major side effects. Wang et al22 demonstrated that nanobubble water curcumin extract (NCE) has the potential to reduce the risk of musculoskeletal injury. 

The current meta-analysis has demonstrated the effectiveness of curcumin in improving joint health. Several studies have reported that curcumin is safe and effective for various joint health conditions, such as joint pain, OA, and RA. Thanawala et al23 demonstrated that a dose of 250 mg of water dispersible turmeric extract can substantially alleviate knee pain and improve joint function in healthy participants without any AEs. Singhal et al27 reported a significant improvement in WOMAC scores in knee OA patients, whereas Shep D et al28 reported a nonsignificant improvement in the KOOS scores of patients with knee OA, using a bioavailable turmeric extract. Atabaki et al,34 Panahi et al,43 Belcaro et al,42 and Rahminia et al44 demonstrated that curcumin at doses of up to 1500 mg/day was effective and significantly reduced inflammation, systemic oxidative burden, and pain without any AEs in patients with OA.

Amalraj et al,29 at doses of 250 mg and 500 mg, and Javadi et al,31 at a dose of 120 mg or 40 mg three times a day evaluated the efficacy of curcumin in relieving the symptoms of RA and reported the safety and efficacy of curcumin in patients with RA. Henrotin et al37 and Nakagawa Y et al39 demonstrated that curcumin at up to 1500 mg/day was effective and significantly reduced inflammation, systemic oxidative burden, and pain without any AEs in patients with OA.

Based on the current literature review of randomized controlled clinical studies, the research team observed that most of the turmeric extract formulations contained approximately 20-40% curcuminoids, whereas the water dispersible turmeric extract, WDTE60N, contained 60% natural curcuminoids. In the randomized, double-blind, placebo controlled, clinical trials for joint health and DOMS, the water dispersible turmeric extract showed clinical benefits at the same single daily dose of 250 mg, 150 mg of curcuminoids, as compared to placebo.20,28

CONCLUSIONS

Turmeric extract and curcumin supplements can be effective adjuncts for the management of musculoskeletal health, with a low incidence of AEs. The water-dispersible turmeric extract, WDTE60N, at a dose of 250 mg per day was found to be more effective than other curcumin products. However, the studies included in the analysis were conducted using diverse doses and treatment durations. Further evaluation using comparisons in future clinical trials can establish the appropriate effective dose of curcumin supplements for the overall maintenance of musculoskeletal health.


