Review Article

Effectiveness of ginger in the management of arthritis- A systematic review of randomized controlled trials

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ABSTRACT

Background/objectives: Arthritis is a chronic, debilitating disease that affects patients' daily lives due to stiffness, pain, and restricted mobility. Natural medicines such as ginger (Zingiber officinale) are reported to improve arthritis symptoms and provide significant pain relief. This review aimed to evaluate the available clinical evidence on ginger's therapeutic role in arthritis as a standalone treatment or an adjunct and to assess its safety profile. **Methods:** This PRISMA-guided systematic review includes randomized controlled trials in which ginger was used as a standalone intervention for pain management in osteoarthritis or rheumatoid arthritis, or that included placebo or control groups. Studies were included if they reported pain relief measured using the Visual Analog Scale (VAS) or the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). We screened articles from six databases: PubMed, SCOPUS, COCHRANE, ScienceDirect, EMBASE, and ClinicalTrials.gov. A total of 613 studies were screened, and seven studies were included in the final analysis. **Results**: Of the seven studies, two used a crossover design, one was open-label, one was a placebo-controlled parallel-group trial, and three were double-blind placebo-controlled trials. Different studies used various measures to assess pain relief after ginger therapy (VAS in two studies, WOMAC in one, KOSS in one, and both the WOMAC and VAS scales in two studies). All but one study has shown the beneficial role of ginger therapy in relieving pain in patients with arthritis. **Conclusion:** Ginger supplementation can be a therapeutic option in managing arthritis symptoms, particularly in improving pain and functional outcomes. The anti-inflammatory and antioxidant properties of ginger's bioactive compounds provide a plausible mechanism for these effects. However, further research is needed to establish optimal dosing regimens, long-term efficacy, and safety profiles. **Protocol Registration:** PROSPERO: CRD42025631420.

Key words: Arthritis, Ginger, Osteoarthritis, Zingiber officinale

Arthritis, particularly osteoarthritis (OA) and rheumatoid arthritis (RA), is a leading, prevalent, and debilitating condition affecting millions of individuals across various age groups globally. [1, 2] These are characterized by inflammation and joint degeneration, causing chronic pain, joint stiffness, disability, and functional impairment, leading to a significantly reduced quality of life. Conventional treatments for arthritis, such as nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and disease-modifying anti-rheumatic drugs (DMARDs), are often used to manage symptoms. However, long-term use of these medications can lead to adverse effects, including gastrointestinal problems, cardiovascular risks, kidney damage, and immunosuppression. [3] These limitations have led to growing interest in complementary and alternative therapies that could reduce symptoms while causing fewer adverse effects. In recent years, there has been growing interest in natural products, Natural Diet Systems (NDS), and herbal remedies as adjunctive or alternative treatments for arthritis. [4, 5] Among the various natural remedies investigated for arthritis, ginger (Zingiber officinale) has emerged as a

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promising candidate. Ginger has long been utilized in traditional medicine for its anti-inflammatory, analgesic, and antioxidant properties. Its bioactive compounds, such as gingerol and shogaols, have been shown to inhibit cyclooxygenase (COX) activity and reduce pro-inflammatory cytokines, making it a potential adjunct treatment for arthritis. [6-9]

As the prevalence of arthritis increases, exploring alternative treatments, such as ginger, could provide significant benefits for patients seeking natural, safer, and more effective solutions. Therefore, we planned this systematic review to comprehensively evaluate and synthesize the existing clinical evidence on the effectiveness of ginger in the management of arthritis. The research question for this systematic review is: "What is the effectiveness of ginger in reducing pain, improving joint function, and managing inflammation in patients with arthritis?" This review aims to evaluate the available clinical evidence on the therapeutic role of ginger in arthritis, its potential as an adjunct to standard treatment, and its safety profile. Given the growing demand for alternative therapies, this systematic review will contribute to the scientific understanding of ginger's role in arthritis management and provide healthcare professionals with valuable insights to inform treatment decisions.

METHODS

To conduct this review, we used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [1]. The studies included were RCTs where patients diagnosed with arthritis (e.g., OA, RA, or both), the ginger (Zingiber officinale) was used as a standalone intervention for pain management, had any placebo or any other control group (e.g., standard care, non-ginger dietary interventions, or pharmacological treatments) and studies reported pain relief (measured using Visual Analog Scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), or other patient-reported outcomes}. PICO elements are presented in Table 1.

Table 1 - PICOS Element

PICOS Element	Details
Population	Patients diagnosed with arthritis (e.g., osteoarthritis, rheumatoid arthritis, or both).
Intervention	Use of ginger (Zingiber officinale) as a standalone intervention for arthritis management.
Comparison	Placebo or any other control group (e.g., standard care, non-ginger dietary interventions, or pharmacological treatments).
Outcome	Pain relief (measured using Visual Analog Scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), or other patient-reported outcomes).

Quasi-randomized controlled studies, prospective and retrospective observational studies, case series, case reports, letters, editorials, comments, animal studies, and non-English literature studies were excluded. Electronic databases, including PubMed, SCOPUS, the Central Cochrane Registry of Controlled Trials (The Cochrane Library), and ScienceDirect, were searched using the details outlined in Table 2. The reference lists of included studies were reviewed for any additional relevant studies. Three investigators (SR, AA, and AA) independently screened the titles, abstracts, and keywords to shortlist the articles. The full-text files were retrieved and evaluated for the final inclusion in the review. The conflicts between the authors were resolved by consensus, and the authors were contacted to address any missing data. The PRISMA flow chart illustrating the study selection process is presented in Figure 1.

Table 2 - Details of search strategy

Database	Search details
PubMed	(("ginger s"[All Fields] OR "zingiber officinale"[MeSH Terms] OR ("zingiber"[All Fields] AND "officinale"[All Fields]) OR "zingiber officinale"[All Fields] OR "ginger"[All Fields] OR "gingers"[All Fields]) AND ("arthritis"[MeSH Terms] OR "arthritis"[All Fields] OR "arthritides"[All Fields] OR "polyarthritides"[All Fields])) AND ((clinical trial[Filter] OR meta-analysis[Filter] OR randomized controlled trial[Filter]) AND (1000/1/1:2024/11/2[pdat]))
SCOPUS	TITLE-ABS-KEY (ginger AND arthritis AND randomized)
ScienceDirect	Title, abstract, keywords: ginger arthritis
COCHRANE	41 Trials matching ginger arthritis in Title, Abstract, and Keyword
EMBASE	'ginger' AND 'arthritis'
ClinicalTrials.gov	ginger arthritis

The details included were study authors, year of publication, country, inclusion/exclusion criteria, sample size in each group, age, gender, formulation and dose of the ginger preparation, placebo or comparator, reported outcomes, and reported adverse events (AEs). The revised JBI critical appraisal tool was used to assess the risk of bias in randomized controlled trials [2].

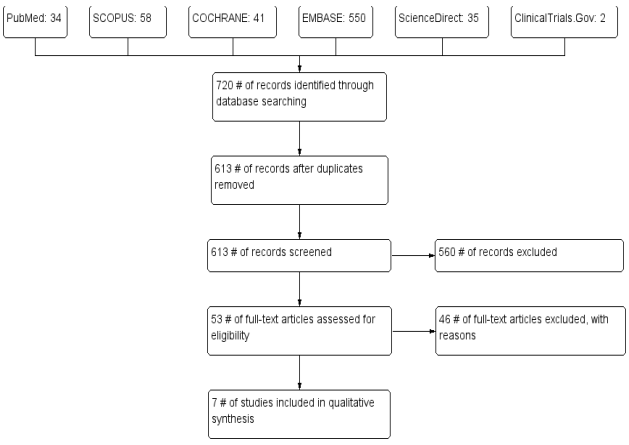

Figure 1: PRISMA flow diagram

RESULTS

Study selection

The search results retrieved 720 articles, and 107 duplicates were removed. Of the remaining 613 articles, 560 were excluded as they did not meet the eligibility criteria. After reading the full texts of 53 articles, 46 were excluded for various reasons, and seven were included in the final analysis (**Figure 1**).

Study characteristics

Of the seven studies, two used a crossover design, one was open-label, one was a placebo-controlled parallel-group trial, and three were double-blind placebo-controlled trials.

Different studies used different measures to assess pain relief after ginger therapy, e.g., the VAS (Visual analog scale) by two studies, the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index scale) by one, the KOSS score (Knee Injury and Osteoarthritis Outcome Score) by one, and both the WOMAC and VAS scales by two studies. The characteristics of the included studies are presented in Table 3. All but one study has shown the beneficial role of ginger therapy in relieving pain in patients with arthritis.

Table 3 - Characteristics of included studies

Study & Authors	Country	Study Type	Participants	Sample Size	Age	Sex	Inclusion Criteria	Exclusion Criteria	Intervention Groups	Outcomes	Follow-up	Remarks
Altman, 2001 [10]	USA	Randomized, Double-blind, Placebo-controlled, Multicenter	Patients with moderate-to-severe knee osteoarthritis	261	Adults (18+ years)	Not specified	OA of the knee with Kellgren & Lawrence grades 2-4, pain on standing between 40-90 mm on a 100 mm VAS	Rheumatoid arthritis, gout, fibromyalgia, cancer, kidney/liver failure, prior corticosteroid injections	Group I: Ginger extract, Group II: Placebo	Significant reduction in knee pain in the ginger extract group	6 weeks	Moderate pain reduction; mild GI side effects in ginger group
Aryaeian, 2019 [11]	Iran	Randomized Double-blind Placebo-controlled Clinical Trial	Active RA patients	70	19-69 years	Male: 7, Female: 63	RA diagnosis, >2 years of disease duration, DMARDs treatment	Myocardial infarction, hyperlipidemia, renal or hepatic dysfunction, smoking, pregnancy	Ginger supplementation (1500 mg/day) vs placebo	Increased FoxP3 expression, reduced T-bet and RORγt expression, reduced DAS-28 score	12 weeks	Ginger showed potential to improve RA symptoms via genetic pathways.
Baek, 2024 [12]	South Korea, China	Randomized, Double-blind, Placebo-controlled Clinical Trial	Patients with mild knee osteoarthritis	100	Range: 50-80 years	Males: 22, Females: 78	Kellgren–Lawrence grades 1-2, pain (VAS 30-70mm) for ≥3 months	Steroid/hyaluronic acid injections in the past 3 months, BMI <18.5 or >35, rheumatoid arthritis, recent fractures, certain chronic diseases	Group 1: Steamed Ginger Extract (0.48g/day), Group 2: Placebo	Significant reduction in pain VAS and K-WOMAC scores in the ginger group	12 weeks	Steamed ginger extract improved OA symptoms without side effects
Blidda l, 2000 [13]	Denmark	Randomized controlled trial	Patients with osteoarthritis (hip or knee)	56	Mean age: 66 years (24–87)	15 men, 41 women	Clinical and radiologically verified osteoarthritis (Kellgren grade 1–4), pain >30 mm on 100 mm VAS	Rheumatoid arthritis, neurological disorders, severe medical diseases, and dementia	EV.ext-33 ginger extract (170 mg t.i.d.), Ibuprofen (400 mg t.i.d.), Placebo	Pain reduction on VAS and Lequesne-index, improved function; Ibuprofen>ginger>placebo	Three 3-week treatment periods with one week washout before the first period	Significant difference between Ibuprofen and ginger; no significant difference between ginger and placebo in the cross-over design
Niempoog, 2012 [14]	Thailand	Double-blind Randomized Controlled Trial	Patients with osteoarthritis of the knee	60	Mean Age: 48.88 years	Males: 7, Females: 53	Clinical diagnosis of osteoarthritis, no knee deformities, no prior knee surgery in the past 6 months	Use of NSAIDs or analgesics 2 weeks before trial, significant knee deformities	Group I: 1g powdered ginger/day, Group II: Placebo	No significant difference in pain relief between ginger and placebo	4 weeks, 8 weeks	Powdered ginger did not provide significant pain relief compared to a placebo
Paramdeep, 2013 [15]	India	Randomized Open	Patients with osteoarthritis of	60	Mean Age: 52.5	Males: 20, Fema	Patients fulfilling ACR criteria for OA diagnosis with	Cardiovascular diseases, hypertension, gastro-	Group I: Diclofenac 50 mg + Placebo, Group II:	Significant improvement in WOMAC and VAS scores	Every 2 weeks till 12 weeks	Ginger had an additive effect with an

		Label Study	the knee		6 years (Range: 35-61)	les: 40	knee pain between 40-90 mm on a 100 mm VAS	duodenal disorders, diabetes mellitus, hepatic or renal impairment, bleeding disorders, pregnancy	Ginger 750 mg + Placebo, Group III: Ginger 750 mg + Diclofenac 50 mg	across all groups, with the best results in Group III		acceptable safety profile
Wigler, 2003 [16]	Israel	Double-blind, Placebo-controlled, Crossover Study	Patients with symptomatic gonarthritis	29	Range: 42-85 years	Males: 6, Females: 23	OA diagnosis based on ACR criteria, Kellgren & Lawrence grades 2-4, pain on movement (VAS ≥ 35mm)	Pregnancy, other rheumatic diseases, recent corticosteroid/hyaluronan injections, anticoagulants (except mini-aspirin), recent orthopedic surgery	Group 1: Ginger extract (250mg, QID) → Placebo, Group 2: Placebo → Ginger extract	Significant reduction in pain and handicap after crossover phase	24 weeks (crossover at 12 weeks) + 24 weeks open study	Ginger extract showed delayed but significant pain relief compared to the placebo

Results of individual studies

In a 6-week, double-blind, placebo-controlled, parallel-group multicentre trial, Altman *et al.*[10] studied 261 patients with knee OA (130 cases in the ginger extract group and 131 cases in the placebo group). Both groups had comparable demographic distributions. The study results showed that 63% of patients in the ginger extract group had a threshold improvement of >15 mm in standing pain, compared with 50% in the placebo group (P = 0.048). The mean reduction in pain was 8.1 mm greater in the ginger extract group (P = 0.005). In further subgroup analyses, the ginger extract group showed higher thresholds of improvement:>20 mm reduction (59% vs. 46%; P = 0.036) and >25 mm reduction (52% vs. 39%; P = 0.035).

Pain after walking 50 feet improved significantly in the ginger extract group, with corresponding improvement in stiffness on the WOMAC scale. Global status assessments were also better in the ginger extract group (P = 0.042); however, no significant change was noted in quality-of-life scores as measured by the Short Form-12 (SF-12) survey. The use of acetaminophen as a rescue medication was comparable between groups, with an average daily intake of 2 tablets. In the ginger extract group, gastrointestinal (GI) AEs (eructation, dyspepsia, and nausea) were more frequent (45% vs 16%), but this difference was not statistically significant.

Aryaeian *et al.* [11] A double-blind, placebo-controlled RCT investigated the effect of ginger supplementation on the expression of inflammatory and immune-related genes in patients with active RA; diagnoses were based on the American College of Rheumatology (ACR) criteria. The authors enrolled 70 participants aged 19–69 years with active RA and randomly assigned them to receive either 1500 mg of ginger powder daily (in capsule form) or a placebo containing wheat flour for 12 weeks. Of these, 63 participants completed the trial, and 7 dropped out due to incomplete supplement intake or medication changes. They showed increased FoxP3 (P < 0.05), GATA-3 (P = 0.061), and PPAR-γ (P = 0.12) gene expression and decreased T-bet gene expression (P = 0.04) in the ginger group compared to the placebo group.

The Disease Activity Score-28 (DAS28-ESR) showed a significant reduction in the ginger group (P = 0.001) and between the two groups (P = 0.003), indicating improved overall disease activity.

Baek *et al.*12, in a double-blind, placebo-controlled RCT, assessed the efficacy and safety of the ginger extract preparation GGE03 for managing mild knee OA. They enrolled 100 subjects (50 patients received 1600 mg/day GGE03 and 50 received a placebo). Baseline characteristics were similar between groups, and 96 participants completed the study; 4 were excluded due to insufficient data. A significant reduction in pain VAS scores (-15.20±5.86 mm) was noted in the GGE03 group than in the placebo group (-3.19±5.56 mm) (p <0.0001). This was maintained at the 6-week follow-up, suggesting a consistent benefit in the GGE03 group. The total K-WOMAC score also decreased significantly in the GGE03 group (-10.00±5.24 vs. -2.66±5.45 points) compared with the placebo group after 12 weeks (p < 0.0001).

Further subscale analyses indicated significant improvements in pain (-3.04±1.81 points), stiffness (-1.37±0.83 points), and physical function (-5.59±3.65 points) in the GGE03 group. At the 6- and 12-week follow-ups, the GGE03 group reported significant improvements in PGA scores compared with the placebo group (p < 0.0001). There was a significant reduction in hs-CRP, ESR, and IL-1β levels in the GGE03 group after 12 weeks, along with a decrease in MMP-9 and an increase in TIMP-1 levels, suggesting potential joint-protective effects of GGE03. A significant improvement in WHOQOL-BREF scores across domains, including physical health, psychological well-being, and social relationships, was observed in the GGE03 group. No serious AEs were reported in either group.

Bliddal *et al.* [13] studied the efficacy and safety of ginger extract (EV.ext-33) compared with ibuprofen and placebo for the treatment of OA. The authors enrolled 75 patients, of whom 56 (41 female, 15 male) completed the study. Twenty patients had hip OA, and 36 had knee OA. The authors found that VAS pain scores significantly improved across all three treatment

arms, with ibuprofen showing the greatest efficacy, followed by ginger extract and placebo.

Acetaminophen consumption as a rescue medication was lower in the ibuprofen group than in the ginger and placebo groups. Functional disability assessment using the Lequesne index showed significant improvement with ibuprofen, followed by the ginger and placebo groups ($P < 0.00005$). 66% of participants preferred ibuprofen, while 14% and 11% preferred ginger extract and a placebo, respectively. There were no significant differences in the range of motion across the treatment groups. A total of 47 AEs were reported in 34 patients, including GI complaints such as dyspepsia, nausea, and changes in stools. Five patients in the ginger group and seven in the ibuprofen group had dyspepsia. Other AEs reported were allergic reactions in three patients (one each in all three groups; however, none of the AEs were severe or life-threatening.

Niempoog *et al.* [14], in a double-blind, placebo-controlled RCT, assessed the efficacy of powdered ginger administered for 8 weeks to manage knee OA symptoms. The authors enrolled 60 patients diagnosed with OA and divided them into the treatment group (30 patients; received 500 mg of powdered ginger BD) and the placebo group (30 patients). Out of these, four patients in the treatment group and seven in the placebo group dropped out. Baseline characteristics were similar in both groups, including the Kellgren-Lawrence (KL) score (2.03±0.75 and 2.16±0.83 in the treatment and placebo groups, respectively) and KOOS scores (72.86±16.41 and 75.24±12.97 in the treatment and placebo groups, respectively). Scores for symptoms (73.63±17.98 and 80.90±12.21), daily activity (78.39±15.84 and 81.71±13.40), sport and recreation activity (60.82±24.40 and 57.88±25.08), and quality of life (QOL) (54.09±26.09 and 50.81±27.39) were comparable in the treatment and placebo groups.

At eight-week follow-up, both groups showed improvement in all subscales, and the placebo group had statistically nonsignificant improvements in symptoms, daily activity, sport and recreation, and QOL scores ($p > 0.05$). The study results suggested that both powdered ginger and placebo led to symptom improvements; however, powdered ginger did not demonstrate superior efficacy compared with placebo. There were no major AEs, and only one patient had heartburn.

Paramdeep *et al.* [15]In an open-label RCT, the efficacy and safety of ginger (Zingiber officinale) powder, both as a standalone treatment and in combination with diclofenac, were evaluated for knee OA. The study includes 60 patients and randomized them into three groups (20 each), group I: Diclofenac 50 mg + placebo capsules (BD), group II: Ginger powder capsules 750 mg + placebo capsules (BD), and Group III: Ginger powder 750 mg + Diclofenac 50 mg (BD). The study duration was 12 weeks, and the rescue medication was Acetaminophen 500 mg for patients with severe pain. The baseline characteristics including mean age, gender, WOMAC, and VAS scores were comparable across the groups. At the 12-week follow-up, a significant improvement was observed in both WOMAC and VAS scores across all groups, (WOMAC - group I: 74.83%, group II: 63.68%, and group III: 79.43% respectively, and VAS - group I: 60.31%, group II: 59.11%, and group III: 66.77% respectively). Further analysis showed that Group III had the maximum improvement in both scores, followed by Groups I and II. AEs included nausea (2 in group II), epigastric distress (2 in group II and 1 in group III), heartburn (2 in group II and 1 in group III), and constipation (1 in group III), with no statistically significant differences.

Wigler *et al.* [16], in a double-blind, placebo-controlled crossover RCT evaluated the efficacy of ginger extract (Zintona EC) versus placebo (containing maltodextrin) in 29 patients (6 men and 23 women) of knee OA. The trial was planned in two phases, each lasting 12 weeks, with a crossover at week 12. Patients who opted to continue ginger extract treatment were followed for an additional 24 weeks. Paracetamol was used as a rescue medication if needed, and its use was restricted before clinical evaluations.

In phase 1 (first 12 weeks), the VAS scores for pain on movement and handicap significantly decreased in both groups, In the Zintona EC group, pain VAS decreased from 76.14 (95% CI: 67.69–84.60) to 41.00 (95% CI: 22.50–59.49) ($P=0.001$), and handicap VAS decreased from 75.86 (95% CI: 68.00–83.72) to 39.72 (95% CI: 22.24–57.22) ($P=0.001$). In the placebo group, pain VAS reduced from 76.87 (95% CI: 71.64–82.09) to 50.00 (95% CI: 33.46–66.53) ($P=0.001$), and handicap VAS decreased from 73.47 (95% CI: 66.66–80.28) to 46.08 (95% CI: 29.75–62.40) ($P=0.002$).

However, the difference between groups was not significant during this phase. In phase 2 (crossover, weeks 13–24) pain and handicap VAS continued to decrease in the group switching from placebo to Zintona EC [means of 9.30 (95% CI: 3.29–15.31) and 10.00 (95% CI: 3.84–16.16), respectively], by week 24. Conversely, the scores increased in the group switching from Zintona EC to placebo, with pain and handicap VAS reaching 82.10 (95% CI: 69.81–94.39) and 80.80 (95% CI: 68.47–93.12), respectively ($P<0.001$). In phase 3 (weeks 25–48) when both groups received Zintona EC, pain and handicap VAS decreased further in the placebo-first group and remained low in the Zintona EC-first group. Although both groups had significant reductions compared to baseline, the difference between groups was not statistically significant.

In phase 1, knee circumference was decreased in both groups; the Zintona EC group (43.25 to 39.36 cm, $P=0.003$) had a greater reduction than the placebo group (41.27 to 38.58 cm, $P<0.001$). During phase 2, knee circumference increased in the Zintona-to-placebo group but continued to decrease in the placebo-to-Zintona group, and in phase 3, both groups showed significant reductions compared to baseline, means of 38.78 cm (95% CI: 34.84–42.72) and 36.38 cm (95% CI: 32.94–39.81), respectively ($P<0.001$). At the 24th week, 10 of 15 patients in

the placebo-to-Zintona group reported >30% reduction in pain and handicap, compared to only 1 patient in the Zintona-to-placebo group (P=0.001), however, no significant difference was noted for >5% reduction in knee circumference. There were no major AEs; however, heartburn led to two dropouts on Zintona EC. Also, 9 patients dropped out during the double-blind phase, and 3 withdrew during the open-label phase.

Risk of bias and quality assessment

JBI Critical Appraisal Checklist for RCT Studies [17] showed that Altman [10], Baek [12], and Wigler [16] had good methodological quality. Followed by Aryaeian [11] Bliddal [13] Niempoog [14] and Paramdeep [15] which had certain limitations (Table 4).

Table 4 - JBI critical appraisal checklist for RCT studies [17]

Study ID	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12	Item 13
Altman, 2001 [10]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Aryaeian, 2019 [11]	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Baek, 2024 [12]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Bliddal, 2000 [13]	Yes	Unclear	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Niempoog, 2012 [14]	Yes	No	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Paramdeep, 2013 [15]	Yes	No	Yes	No	No	Unclear	No	Yes	Yes	No	Yes	Yes	Yes
Wigler, 2003 [16]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

DISCUSSION

Ginger (Zingiber officinale), a plant-based phenolic compound, has been used to treat many diseases since ancient times. Europeans even went so far as to call it "elderly medicine". Ballester P *et al.* suggested that the bioactive compounds of ginger (6-shoagol, zingerone, and 8-shoagol) play a promising role in the inflammatory process and its signaling pathways in human and animal models, reducing key symptoms of inflammatory diseases such as arthritis. 6-gingerol demonstrated a protective, attenuating effect on neutrophil extracellular trap release in response to phosphodiesterase inhibition in lupus patients. Ginger decreases NF-kβ in psoriasis, and its short-term administration may be an alternative adjuvant treatment. Ginger may serve a role in supplementation and protection against cancer. Furthermore, when receiving chemotherapy, ginger may help reduce some treatment-related symptoms. [18]

Ginger contains various bioactive compounds, such as gingerols, shogoals, and paradols, which contribute to its analgesic and anti-inflammatory properties. [19] Ginger acts by various pathways, like inhibiting chemokines, pro-inflammatory cytokines, NF-κB, and MAPK, and inducing anti-inflammatory mediators (IL-4, IL-10), making it a suitable therapeutic option for arthritis. Shogoal also prevents bone erosion by inhibiting RANKL-induced osteoclast differentiation. [20] Arthritis, being an autoimmune condition, requires the downregulation of immunity.

This is achieved by the suppression of genes encoding retinoic acid receptor-related orphan nuclear receptor gamma, NF-κB, and T-bet, which are involved in autoimmunity. On the other hand, elevated levels of the peroxisome proliferator-activated receptor, GATA3, and forkhead box P3 genes were observed. Thus, these expressions exhibited by ginger molecules provide the backbone for ginger use in treating OA and RA. The cyclooxygenase- and 5-lipoxygenase-inhibitory potential of ginger also attracted researchers involved in rheumatology. [20]

Although ginger therapy has been shown in multiple small studies to alleviate arthritis symptoms such as pain, stiffness, and swelling by modulating inflammatory pathways, results have been inconsistent, and the clinical evidence remains insufficient to establish firm therapeutic guidelines. There is a lack of robust, synthesized evidence to confirm the efficacy and safety of ginger as a treatment for arthritis. Various studies differ in study design, dosing regimens, types of arthritis, and outcome measures, making it difficult to draw definitive conclusions. [10, 13-16]

Furthermore, many studies have small sample sizes or inconsistent methodologies, limiting their generalizability and reliability. A previous meta-analysis of 593 patients from five randomized controlled trials (RCTs) showed a statistically significant reduction in pain and disability following ginger intake (P = 0.005 and P = 0.01, respectively). [21] However, this study was published in 2015, and more studies have been published in the last 10 years. [12, 22-25]

In this review, we demonstrated ginger's efficacy in reducing pain, improving joint function, and managing inflammation in patients with arthritis. Bliddal *et al.* [13], conducted a randomized, placebo-controlled crossover study of ginger extracts and ibuprofen. They found ibuprofen to be the most effective for controlling pain, followed by ginger extract and the placebo. In the first phase (before the crossover), both ibuprofen and ginger extracts were more effective at relieving

pain than the placebo. Wigler et al. in Israel found that ginger extract (Zintona EC) significantly reduced pain in patients with symptomatic gonarthritis after 24 weeks of treatment compared with placebo.

Only mild GI symptoms were recorded in a few patients, and ginger extracts showed a remarkable safety profile. [16] Aryaeian *et al.* [11] showed that ginger reduces inflammatory factors, hs-CRP, and IL-1β gene expression in patients with active RA, and ginger might decrease inflammation by reducing the production of some inflammatory markers. They reported significantly reduced RORγt and T-bet gene expression and improved FoxP3 gene expression. [11] Several other studies have investigated the effects of ginger on arthritis symptoms. [14, 15]. In a recent study, Baek *et al.* (2024) found that steamed ginger extract (GGE03) significantly improved joint pain and function in subjects with mild knee OA over 12 weeks. This contributes to a growing body of evidence supporting the potential benefits of ginger in managing arthritis symptoms, particularly in knee OA. [12]

Bartels *et al.* (2015) conducted a meta-analysis including 593 patients from five RCTs to examine the efficacy of ginger for the symptomatic treatment of OA. The authors found that ginger was modestly efficacious and reasonably safe for the treatment of OA. The authors reported that patients receiving ginger were more than twice as likely to discontinue treatment due to adverse effects as those receiving a placebo; however, the overall safety profile was favorable. [21] Ribel-Madsen *et al.* (2012) investigated the effects of ginger extract on synovial fluid and serum samples from OA patients and found that it reduced the production of inflammatory mediators in both synovial fluid and serum, suggesting a potential mechanism for its anti-inflammatory effects in osteoarthritis. 26

Recent animal studies have demonstrated improved results when 6-gingerol was incorporated with a nanostructured lipid carrier (NLC), a novel drug delivery method. It was further noted that this novel combination not only showed improved results but also alleviated arthritis-related lesions. However, the results are limited to animal studies only and thus require further research. Researchers have incorporated traditional medicines like ginger and mustard oil with a relatively newer drug delivery system- the transdermal patch and demonstrated improved symptomatic relief in arthritis patients. [27]

Thus, *Zingiber officinale* has shown promising results in controlling arthritis symptoms, with mild to minimal adverse effects, such as a pungent taste, GI symptoms like dyspepsia, nausea, changes in stool, heartburn, and allergies. It is important to note that while these studies provide promising results, there are some limitations to consider. The sample sizes in many of these studies are relatively small, and treatment durations vary across studies.

Also, the optimal dosage and form of ginger supplementation for arthritis management have not been established. The long-term effects of ginger supplementation on arthritis progression and joint health require further investigation. Further large-scale, multicenter trials are necessary to describe the effects of ginger across age groups, genders, and ethnicities, and to understand the potency and side effects of ginger and its by-products.

CONCLUSION

Our study concludes that ginger supplementation may be a promising natural approach for managing arthritis symptoms, particularly in improving pain and functional outcomes in patients with knee osteoarthritis. The anti-inflammatory and antioxidant properties of ginger's bioactive compounds provide a plausible mechanism for these effects. However, further research is needed to establish optimal dosing regimens, long-term efficacy, safety profiles, methods of drug delivery, and the combination of ginger products with NSAIDs. Large-scale, multicentre clinical trials would be valuable in confirming these findings and potentially supporting the integration of ginger supplementation into comprehensive arthritis management strategies. Additionally, overcoming the pungent taste of ginger would make it more palatable and acceptable to patients.

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