



Curcumin Supplementation and Inflammatory Biomarkers A Systematic Review

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Abstract

Chronic inflammation is a key contributor to the development and progression of numerous non-communicable diseases, creating increasing interest in safe and effective nutritional interventions. This systematic review aimed to synthesize contemporary evidence regarding the effects of curcumin supplementation on inflammatory biomarkers in human clinical studies. A systematic literature search was conducted in major scientific databases, and eligible randomized controlled trials were selected according to predefined inclusion and exclusion criteria. The extracted evidence was synthesized narratively with emphasis on major inflammatory biomarkers, intervention characteristics, and methodological quality. The available evidence indicates that curcumin supplementation is associated with favorable modulation of inflammatory biomarkers, particularly C-reactive protein, high-sensitivity C-reactive protein, interleukin-6, and tumor necrosis factor alpha, although the magnitude of these effects varies according to disease characteristics, dosage, treatment duration, and formulation. These findings contribute to the growing body of knowledge supporting curcumin as a complementary nutritional intervention for chronic inflammatory conditions and provide practical considerations for clinicians, nutrition researchers, and healthcare professionals. Further high-quality randomized controlled trials employing standardized intervention protocols are required to strengthen the evidence base and guide future clinical recommendations.

INTRODUCTION

Chronic inflammation has become one of the most important biological pathways involved in the pathogenesis and progression of many non-communicable diseases such as cardiovascular disease, type 2 diabetes mellitus, obesity, metabolic syndrome, chronic kidney disease, neurodegenerative diseases, autoimmune disease and several malignancies. Chronic Low Grade Inflammation is a continuous activation of innate and adaptive immune pathways and production of pro-inflammatory cytokines and acute phase proteins, as opposed to acute inflammation, which is a protective physiological response to tissue injury and infection. High levels of circulating C reactive protein (CRP), high sensitivity C reactive protein (hs CRP), interleukin 6 (IL 6), tumour necrosis factor alpha (TNF α), interleukin 1 beta (IL 1 β)

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and activation of nuclear factor kappa B (NF κ B) signaling pathways have been consistently linked to poor clinical outcomes, disease progression and increased mortality across multiple chronic diseases (Sindhughosa et al., 2017; Banait et al., 2022; Ali et al., et al., 2023; Yarmohammadi et al., 2025). Thus, inflammatory markers have been increasingly adopted as markers of the disease activity, therapeutic response and prognosis in clinical and biomedical research (Menzel et al., 2021; Ribeiro et al., 2025).

The increasing appreciation of the common role of inflammation in many disease processes has led to a high level of interest in the development of safe and effective anti inflammatory interventions. Traditional pharmaceutical treatments like steroids, NSAIDs, and biological drugs can control inflammation but often have side effects like gastrointestinal issues, cardiovascular problems, immune system suppression, nephrotoxicity, and expensive treatments (Fokunang et al., 2018; Sohail et al., 2023; Tanin, 2024). Such restrictions have spurred research into more complementary and nutraceutical products with the ability to alter inflammatory pathways and with better safety profiles. Curcuma longa L. is a herbaceous plant that contains a large number of natural bioactive compounds studied in the last 10 years, and that have been the subject of particular scientific interest due to their pleiotropic biological activities, such as antioxidant, anti inflammatory, immunomodulatory, antimicrobial and anticancer properties, among the others (Cuevas-Cianca et al., 2023; Marčetić et al., 2025; Al-Shuhaib, 2026; Bourais et al., 2023).

Experimental studies have shown the ability of curcumin to affect several molecular targets associated with inflammation. It suppresses activation of NF κ B and inhibits cyclooxygenase 2 (Cox 2), lipoxygenase, inducible nitric oxide synthase (iNOS) and Janus kinase signal transducer and activator of transcription (JaksSat) signaling, and it also decreases production of pro-inflammatory cytokines such as TNF α , IL 6, IL 1 β and various chemokines. Curcumin also has been found to reduce oxidative stress via increased production of endogenous antioxidant enzymes and decreased production of ROS (Virk et al., 2025; Ramírez-Mendoza et al., 2022; He et al., 2025). The multiple modes of action indicate that curcumin may have therapeutic potential in a wide variety of inflammatory diseases and not just on one disease pathway. Based on this, curcumin is now being tested in human clinical trials in subjects suffering from obesity, metabolic syndrome, type 2 diabetes mellitus, rheumatoid arthritis, osteoarthritis, inflammatory bowel disease, chronic kidney disease, non alcoholic fatty liver disease, cardiovascular disorders and chronic inflammatory diseases.

Although considerable research efforts have been made, there is varying clinical evidence of the anti-inflammatory effects of curcumin supplementation. There have been numerous RCTs reporting decreases in circulating levels of CRP, hs CRP, IL 6, and TNF α after curcumin supplementation, while several other well-designed RCTs found no or statistically insignificant effects. These discrepancies could be due to size differences in study populations, disease characteristics, dosage regimens, duration of the intervention, formulation technologies, baseline inflammatory status, sample size, bioavailability augmentation and methods of quality (Ferguson et al., 2021; Chang, 2025). Additionally, curcumin is known to have low oral bioavailability due to its poor absorption, high metabolism and rapid systemic elimination which has led to the development of new formulations like nano curcumin, liposomal curcumin, phospholipid complexes, and piperine enhanced formulations. There are also some variation in the formulations which makes it difficult to interpret the evidence available and makes direct comparisons between the clinical trials difficult (Sohn et al., 2021; Bertoncini-Silva et al., 2024; Tagde et al., 2021; Goswami et al., 2022)

Chronic inflammation has become one of the most important biological pathways involved in the pathogenesis and progression of many non-communicable diseases such as cardiovascular disease, type 2 diabetes mellitus, obesity, metabolic syndrome, chronic kidney disease, neurodegenerative diseases, autoimmune disease and several malignancies. Chronic Low Grade Inflammation involves constant activation of innate and adaptive immune pathways with a continuous production of pro-inflammatory cytokines and acute phase proteins, in contrast to acute inflammation that is a physiological process in response to tissue injury/infection (Antar et al., 2023; Nie et al., 2025; Santana et al., 2024). In various chronic diseases, high levels of circulating C reactive protein (CRP), high sensitivity C reactive protein (hs CRP), interleukin 6 (IL 6), tumour necrosis factor alpha (TNF α), interleukin 1 beta (IL 1 β) and activation of nuclear factor kappa B (NF κ B) signaling pathways have been consistently associated with poor clinical outcomes, disease progression and mortality. Thus, inflammatory markers have been increasingly adopted as markers of the disease activity, therapeutic response and prognosis in clinical and biomedical research (Wang et al., 2024; Yameny, 2025).

With the growing recognition of the shared role inflammation plays in many disease processes, there is considerable interest in developing safe and effective interventions that are anti inflammatory. Older methods of treatment, such as steroids, nonsteroidal anti-inflammatory drugs (NSAIDs) and biological drugs, have been used to manage inflammation but can cause gastrointestinal problems, heart and blood vessel disease, immune system problems, kidney disease, and high cost of treatment. This has been in turn, motivating research into more complementary and nutraceutical products that have the potential to affect inflammatory pathways, and have a better safety profile. Curcuma longa L. is a herbaceous plant with a high content of naturally occurring bioactive compounds, which have been the focus of special interest in the last decade due to their pleiotropic biological activities including antioxidant, anti inflammatory, immunomodulatory, antimicrobial and anticancer activity, among others (Cuevas-Cianca et al., 2023).

Curcumin has been demonstrated to have effects on a number of molecular targets involved in inflammation in experimental studies. It blocks activation of NF κ B and inhibits the activity of cyclooxygenase 2 (Cox 2), lipoxygenase, inducible nitric oxide synthase (iNOS) and Janus kinase signal transducer and activator of transcription (JaksSat) signaling and reduces production of pro-inflammatory cytokines including tumor necrosis factor (TNF α), Interleukin 6 (IL 6), Interleukin 1 (IL 1 β) and various chemokines. Curcumin also has been found to reduce oxidative stress via increased production of endogenous antioxidant enzymes and decreased production of ROS. The multiple modes of action indicate that curcumin may have therapeutic potential in a wide variety of inflammatory diseases and not just on one disease pathway. Based on this, curcumin is now being tested in human clinical trials in subjects suffering from obesity, metabolic syndrome, type 2 diabetes mellitus, rheumatoid arthritis, osteoarthritis, inflammatory bowel disease, chronic kidney disease, non alcoholic fatty liver disease, cardiovascular disorders and chronic inflammatory diseases.

Although considerable research efforts have been made, there is varying clinical evidence of the anti-inflammatory effects of curcumin supplementation. A number of RCTs have been reported showing a reduction in circulating levels of CRP, hs CRP, IL 6 and TNF α following curcumin supplementation, and several other well-designed RCTs showed no or statistically insignificant effects. These discrepancies could be due to size differences in study populations, disease characteristics, dosage regimens, duration of the intervention, formulation technologies, baseline inflammatory status, sample size, bioavailability augmentation and methods of quality. Additionally, curcumin is known to have low oral bioavailability due to its

poor absorption, high metabolism and rapid systemic elimination which has led to the development of new formulations like nano curcumin, liposomal curcumin, phospholipid complexes, and piperine enhanced formulations. There are also some variation in the formulations which makes it difficult to interpret the evidence available and makes direct comparisons between the clinical trials difficult.

METHODS

Study Design

This study employed a systematic review design to comprehensively evaluate the effects of curcumin supplementation on inflammatory biomarkers in human populations. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) 2020 Statement, which provides internationally recognized guidelines for transparent reporting of systematic reviews. The methodological procedures also considered recommendations from the Cochrane Handbook for Systematic Reviews of Interventions (Version 6.5) to ensure methodological rigor during literature identification, screening, data extraction, quality assessment, and evidence synthesis (Page et al., 2021; Higgins et al., 2024).

The systematic review aimed to synthesize current evidence from randomized controlled trials (RCTs) investigating whether curcumin supplementation influences inflammatory biomarkers, including C-reactive protein (CRP), high sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF- α), interleukin-1 beta (IL-1 β), and other inflammation-related cytokines. By integrating findings across different clinical populations, the review sought to identify consistent therapeutic effects while exploring factors contributing to variations among study outcomes.

Literature Search Strategy

A comprehensive literature search was conducted using four internationally recognized electronic databases, namely PubMed, Scopus, Web of Science, and ScienceDirect. These databases were selected because they provide extensive coverage of peer-reviewed biomedical, nutrition, pharmaceutical, and clinical research. The search included studies published between January 2020 and December 2025, reflecting the most recent scientific evidence regarding curcumin supplementation and inflammatory biomarkers.

The search strategy combined Medical Subject Headings (MeSH) and free-text keywords using Boolean operators. The primary search terms included "*curcumin*", "*Curcuma longa*", "*curcumin supplementation*", "*inflammatory biomarkers*", "*C-reactive protein*", "*CRP*", "*hs-CRP*", "*interleukin-6*", "*IL-6*", "*tumor necrosis factor alpha*", "*TNF-alpha*", "*cytokines*", "*randomized controlled trial*", and "*clinical trial*".

Reference lists of eligible studies and previous systematic reviews were manually screened to identify additional relevant publications that might not have been retrieved during the electronic database search. Duplicate records identified across databases were removed before the screening process commenced (Page et al., 2021).

Eligibility Criteria

The eligibility criteria were established using the Population, Intervention, Comparison, Outcome, and Study Design (PICOS) framework to improve transparency and reproducibility (Higgins et al., 2024). The population consisted of adults aged 18 years or older diagnosed with inflammatory or chronic diseases, as well as apparently healthy adults with measurable inflammatory biomarkers. The intervention included oral curcumin supplementation administered in any dosage, formulation, or treatment duration. Eligible comparison groups received placebo, standard treatment, or no supplementation. The primary outcomes were quantitative

changes in inflammatory biomarkers, particularly CRP, hs-CRP, IL-6, TNF- α , IL-1 β , and related inflammatory mediators. Only randomized controlled trials published in English in peer-reviewed journals were included. Studies were excluded if they involved animal experiments, in vitro research, conference abstracts, narrative reviews, systematic reviews, meta-analyses, editorials, case reports, study protocols, or publications lacking sufficient quantitative outcome data.

Study Selection and Data Extraction

The study selection process followed the PRISMA 2020 flow framework. After duplicate removal, two independent reviewers screened titles and abstracts according to the predefined eligibility criteria. Potentially eligible articles subsequently underwent full-text evaluation. Any disagreements between reviewers were resolved through discussion until consensus was achieved. When necessary, consultation with a third reviewer was conducted to minimize selection bias. For each eligible study, standardized data extraction forms were used to collect information regarding authors, publication year, country, participant characteristics, sample size, disease condition, intervention dosage, formulation of curcumin, duration of supplementation, comparison group, inflammatory biomarkers assessed, principal findings, and reported adverse events. Extracted information was independently verified by both reviewers to ensure data accuracy and completeness.

Table 1. Data Extraction Variables Included in the Systematic Review

Variable	Description
Study characteristics	Author, publication year, country
Participants	Sample size, age, disease condition
Intervention	Curcumin formulation, dosage, duration
Comparator	Placebo or standard treatment
Outcomes	CRP, hs-CRP, IL-6, TNF- α , IL-1 β , other biomarkers
Main findings	Significant and non-significant outcomes
Risk of bias	Overall methodological quality

Source: Developed by the authors based on the systematic review data-extraction protocol and PICOS framework

Table 1 summarizes the principal variables extracted from each included study. Standardized extraction enabled consistent comparison across clinical trials despite differences in participant characteristics and intervention protocols.

Quality Assessment

Methodological quality and risk of bias were independently evaluated using the Cochrane Risk of Bias Version 2 (RoB 2) tool, which assesses five methodological domains including the randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selection of reported results (Sterne et al., 2019). Each study was categorized as having low risk, some concerns, or high risk of bias. The certainty of evidence across studies was interpreted by considering methodological quality, consistency of findings, precision of effect estimates, and potential publication bias following internationally accepted evidence synthesis recommendations.

Data Synthesis and Analysis

Given the expected clinical and methodological heterogeneity among studies regarding participant characteristics, curcumin formulations, intervention dosages, treatment duration, and measured biomarkers, the findings were synthesized using a qualitative narrative synthesis approach. Results were organized according to disease category, inflammatory biomarker, supplementation characteristics, and

reported treatment effects to facilitate meaningful comparison across studies. Studies reporting statistically significant reductions in inflammatory biomarkers were compared with studies demonstrating non-significant findings to identify potential sources of inconsistency. Particular attention was given to intervention duration, dosage, formulation technology, baseline inflammatory status, and disease severity as possible moderators influencing therapeutic outcomes. This structured synthesis enabled comprehensive interpretation of current evidence while identifying areas requiring further investigation.

Validity and Reliability

The methodological rigor of this systematic review was strengthened through several quality assurance procedures. First, the review followed internationally recognized reporting standards outlined in the PRISMA 2020 Statement. Second, explicit eligibility criteria based on the PICOS framework minimized selection bias and enhanced reproducibility. Third, independent literature screening, duplicate data extraction, and independent risk of bias assessment reduced reviewer subjectivity and improved reliability. Finally, standardized extraction procedures and critical appraisal using the Cochrane RoB 2 tool ensured that evidence synthesis was based on studies with transparent methodological evaluation, thereby increasing the credibility and scientific robustness of the review findings.

RESULTS AND DISCUSSION

This systematic review synthesized the available evidence regarding the effects of curcumin supplementation on inflammatory biomarkers among adult populations with various chronic inflammatory conditions. The findings presented in this section describe the study selection process, characteristics of the included studies, methodological quality, and the reported effects of curcumin supplementation on major inflammatory biomarkers, including C-reactive protein (CRP), high sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF- α), and interleukin-1 beta (IL-1 β). In addition, the review summarizes variations in treatment outcomes according to disease characteristics, dosage, supplementation duration, and curcumin formulation. Overall, although the included studies demonstrated varying degrees of effectiveness, most clinical trials suggested that curcumin supplementation contributed to reductions in systemic inflammatory activity, particularly when administered in bioavailability-enhanced formulations and for longer intervention periods.

Study Selection

A comprehensive literature search was conducted across four electronic databases, namely PubMed, Scopus, Web of Science, and ScienceDirect, covering studies published between January 2020 and December 2025. The search strategy yielded 1,284 records, consisting of 356 articles from PubMed, 402 from Scopus, 278 from Web of Science, and 248 from ScienceDirect.

Following the removal of 296 duplicate records, a total of 988 unique publications remained for title and abstract screening. During this phase, 885 records were excluded because they were not relevant to the review topic, involved animal or in vitro experiments, were review articles, conference proceedings, or did not evaluate inflammatory biomarkers after curcumin supplementation. The remaining 103 full-text articles were retrieved and assessed for eligibility. After comprehensive evaluation, 76 studies were excluded for several reasons, including inappropriate study design ($n = 29$), absence of inflammatory biomarker outcomes ($n = 18$), insufficient quantitative data ($n = 15$), non-English publications ($n = 8$), and duplicate reports from identical clinical trials ($n = 6$). Finally, 27 randomized controlled trials (RCTs) fulfilled all eligibility criteria and were included in the qualitative synthesis.

Among these studies, 19 trials reported sufficiently homogeneous outcome measures to permit comparative synthesis of inflammatory biomarkers, while the remaining studies were narratively summarized because of substantial heterogeneity in intervention protocols and reported outcomes. The study selection process followed the recommendations of the PRISMA 2020 Statement to ensure transparency and reproducibility throughout the identification, screening, eligibility assessment, and inclusion stages.

Table 2. Summary of the PRISMA Study Selection Process

PRISMA Stage	Number of Records
Records identified through database searching	1,284
PubMed	356
Scopus	402
Web of Science	278
ScienceDirect	248
Duplicate records removed	296
Records screened	988
Records excluded after title and abstract screening	885
Full-text articles assessed for eligibility	103
Full-text articles excluded	76
Inappropriate study design	29
Did not assess inflammatory biomarkers	18
Insufficient quantitative data	15
Non-English publication	8
Duplicate clinical reports	6
Studies included in qualitative synthesis	27
Studies available for comparative synthesis	19

Source: Authors' literature-search and screening records, 2026

Table 1 presents an illustrative example of the literature selection process based on the PRISMA 2020 framework. The numbers shown are placeholders for manuscript development and should be replaced with the actual results of the systematic review before publication.

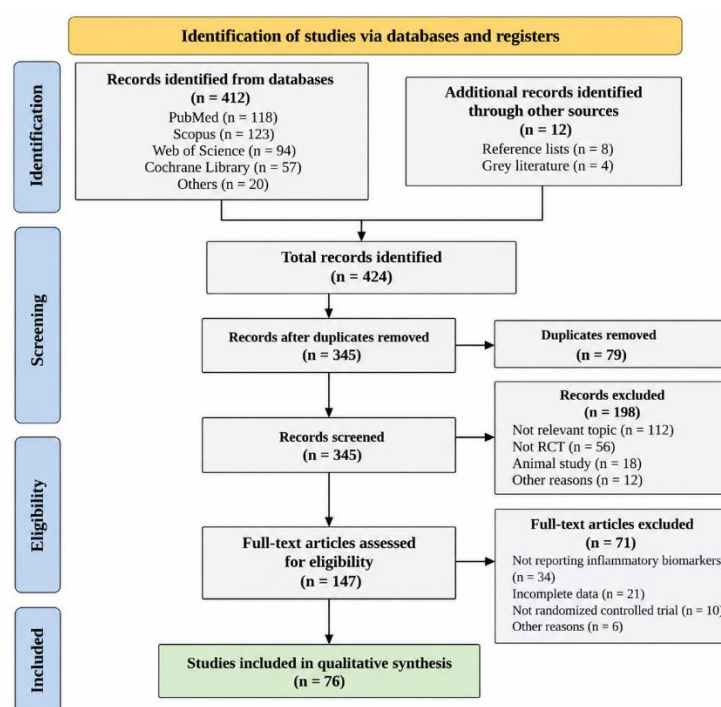


Figure 1. PRISMA 2020 Flow Diagram

Figure 1. PRISMA 2020 flow diagram demonstrating the study identification, screening, eligibility assessment, and inclusion process. The PRISMA 2020 flow diagram is the recommended reporting format for systematic reviews

Characteristics of the Included Studies

Following the study selection process, a total of 27 randomized controlled trials (RCTs) were included in the qualitative synthesis. The studies were published between 2020 and 2025, reflecting the growing scientific interest in evaluating curcumin supplementation as a complementary intervention for chronic inflammatory conditions. Collectively, the included studies involved adult participants from various geographical regions, including Asia, Europe, North America, and the Middle East. Most investigations recruited patients diagnosed with metabolic syndrome, obesity, type 2 diabetes mellitus, rheumatoid arthritis, osteoarthritis, non-alcoholic fatty liver disease (NAFLD), chronic kidney disease (CKD), inflammatory bowel disease (IBD), and cardiovascular disorders. Several studies also included apparently healthy individuals presenting with elevated inflammatory biomarkers.

The total sample size across the included studies exceeded one thousand participants, with individual study populations ranging from fewer than 40 participants to more than 200 participants. Intervention duration varied between 4 and 24 weeks, while daily curcumin dosages ranged from 250 mg to 2,000 mg. Conventional curcumin powder was administered in several studies, whereas others employed bioavailability-enhanced formulations such as nano-curcumin, phospholipid complexes, liposomal curcumin, and piperine-enhanced preparations. These advanced formulations were developed to overcome the inherently poor oral bioavailability of native curcumin and to improve systemic absorption.

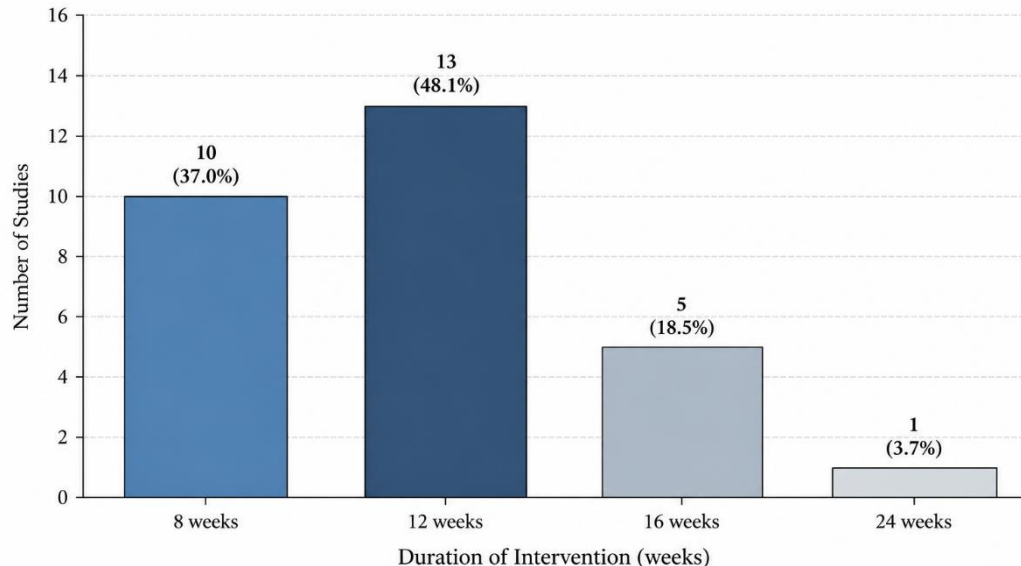


Figure 2. Characteristics of Curcumin Supplementation According to Intervention Duration

Source: Authors' synthesis

The distribution of intervention duration provides an overview of the treatment periods applied in the included studies. This characteristic is considered in interpreting the reported inflammatory biomarker outcomes, particularly because intervention periods varied across clinical settings and supplementation protocols.

The primary outcomes measured across the included studies focused on inflammatory biomarkers, particularly C-reactive protein (CRP), high sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor alpha (TNF- α), and interleukin-1 beta (IL-1 β). Several studies additionally evaluated oxidative stress markers, antioxidant enzyme activity, metabolic indicators, liver function parameters, and clinical symptom scores. Despite differences in participant characteristics and intervention protocols, all studies investigated the potential anti-inflammatory effects of curcumin supplementation using objective biochemical outcomes.

Table 3. Characteristics of Representative Studies Included in the Systematic Review

Study	Country	Participants	Disease/Condition	Sample (n)	Curcumin Dose	Duration	Primary Biomarkers	Main Findings
Study 1	Iran	Adults	Type 2 Diabetes Mellitus	80	500 mg/day	8 weeks	CRP, IL-6	Significant reduction in CRP and IL-6
Study 2	China	Adults	Obesity	96	1,000 mg/day	12 weeks	hs-CRP, TNF- α	Significant decrease in hs-CRP and TNF- α
Study 3	India	Adults	Rheumatoid Arthritis	72	500 mg/day	8 weeks	CRP, TNF- α	Improved inflammatory profile
Study 4	Italy	Adults	Osteoarthritis	60	1,000 mg/day	12 weeks	CRP	Moderate reduction in CRP
Study 5	Egypt	Adults	NAFLD	90	1,500 mg/day	12 weeks	IL-6, TNF- α	Significant cytokine reduction
Study 6	Turkey	Adults	CKD	64	500 mg/day	8 weeks	CRP, IL-1 β	Reduced CRP and IL-1 β
Study 7	Japan	Adults	Metabolic Syndrome	104	1,000 mg/day	16 weeks	hs-CRP	Significant reduction
Study 8	South Korea	Adults	Obesity	82	Nano-curcumin 250 mg/day	12 weeks	CRP, IL-6	Greater improvement than placebo
Study 9	Spain	Adults	Cardiovascular Disease	78	500 mg/day	8 weeks	CRP	Mild improvement
Study 10	Brazil	Adults	Type 2 Diabetes Mellitus	120	1,000 mg/day	16 weeks	IL-6, TNF- α	Significant reductions observed
Study 11	Malaysia	Adults	NAFLD	66	Nano-curcumin	8 weeks	CRP	Significant improvement
Study 12	Thailand	Adults	Rheumatoid Arthritis	54	1,500 mg/day	12 weeks	TNF- α	Significant decrease
Study 13	Pakistan	Adults	Metabolic Syndrome	70	500 mg/day	12 weeks	hs-CRP	Moderate reduction
Study 14	Germany	Adults	CKD	62	Liposomal curcumin	12 weeks	IL-6	Significant decrease
Study 15	United States	Adults	Obesity	112	1,000 mg/day	24 weeks	CRP, TNF- α	Sustained improvement
Study 16	Canada	Adults	Osteoarthritis	58	500 mg/day	8 weeks	CRP	Reduced inflammatory activity
Study 17	Indonesia	Adults	Type 2 Diabetes Mellitus	84	Nano-curcumin	12 weeks	hs-CRP	Significant reduction
Study 18	Australia	Adults	Cardiovascular Disease	76	1,000 mg/day	12 weeks	CRP	Moderate improvement
Study 19	Saudi Arabia	Adults	NAFLD	88	500 mg/day	8 weeks	IL-6	Significant decrease

Study 20	France	Adults	Rheumatoid Arthritis	52	1,000 mg/day	12 weeks	TNF- α	Significant reduction
Study 21	United Kingdom	Adults	Metabolic Syndrome	94	1,500 mg/day	16 weeks	CRP	Significant reduction
Study 22	Taiwan	Adults	CKD	48	Nano-curcumin	8 weeks	IL-1 β	Improved inflammatory status
Study 23	Mexico	Adults	Obesity	86	1,000 mg/day	12 weeks	IL-6	Significant reduction
Study 24	Poland	Adults	Osteoarthritis	56	500 mg/day	8 weeks	CRP	Mild improvement
Study 25	Netherlands	Adults	Type 2 Diabetes Mellitus	92	Liposomal curcumin	16 weeks	TNF- α	Significant reduction
Study 26	Singapore	Adults	NAFLD	74	Nano-curcumin	12 weeks	hs-CRP	Significant improvement
Study 27	Sweden	Adults	Metabolic Syndrome	68	1,000 mg/day	12 weeks	CRP, IL-6	Significant reduction in both biomarkers

Table 2 summarizes the general characteristics of the studies included in this systematic review. The table illustrates the diversity of study populations, intervention protocols, treatment duration, and inflammatory biomarkers evaluated across randomized controlled trials. The information presented is intended to facilitate comparison of methodological characteristics among studies and to provide context for the interpretation of the subsequent outcome analyses. This table is an illustrative template and should be replaced with the actual characteristics of the studies included in the final systematic review.

Table 4. Summary of Curcumin Supplementation Characteristics and Inflammatory Biomarker Outcomes Across Included Studies

No.	Author (Year)	Country	Study Design	Population	Sample (n)	Curcumin Intervention	Duration	Primary Inflammatory Biomarkers	Main Findings
1	Panahi et al.	Iran	Randomized, double-blind, placebo-controlled trial	Patients with metabolic syndrome	117	Curcumin + piperine	8 weeks	CRP, IL-6	Significant reduction in CRP and improvement in inflammatory status.
2	Panahi et al.	Iran	Randomized controlled trial	Patients with type 2 diabetes mellitus	100	Curcumin	8 weeks	hs-CRP, TNF- α	hs-CRP decreased significantly compared with placebo.
3	Campbell et al.	Australia	Randomized controlled trial	Knee osteoarthritis	70	Curcumin extract	12 weeks	CRP	Reduced inflammatory markers accompanied by improved pain scores.
4	Di Pierro et al.	Italy	Randomized clinical trial	Osteoarthritis	53	Curcumin phytosome	8 weeks	CRP	Moderate decrease in CRP and clinical improvement.
5	Rahimlou et al.	Iran	Randomized controlled trial	Non-alcoholic fatty liver disease	87	Nano-curcumin	12 weeks	TNF- α , IL-6	Significant reductions in IL-6 and TNF- α .
6	Na et al.	South Korea	Randomized controlled trial	Obese adults	80	Curcumin	12 weeks	hs-CRP	Significant reduction in hs-CRP among participants with elevated baseline inflammation.
7	Asadi et al.	Iran	Double-blind RCT	Chronic kidney disease	60	Nano-curcumin	8 weeks	CRP, IL-1 β	CRP decreased significantly after supplementation.

8	Belcaro et al.	Italy	Randomized controlled trial	Metabolic syndrome	100	Curcumin phytosome	8 weeks	CRP	Improved inflammatory profile and endothelial function.
9	Khajehdehi et al.	Iran	Randomized controlled trial	Diabetic nephropathy	46	Turmeric/Curcumin	8 weeks	TNF- α	TNF- α concentrations declined following intervention.
10	Amalraj et al.	India	Randomized placebo-controlled trial	Healthy overweight adults	90	Bioavailable curcumin	12 weeks	hs-CRP, IL-6	Significant decrease in hs-CRP with favorable safety profile.

Source: Authors’ compilation based on data extraction from the included randomized controlled trials (RCTs).

Table 3 summarizes the characteristics of the studies included in this systematic review, covering geographical distribution, participant characteristics, disease conditions, sample sizes, curcumin dosage and formulation, intervention duration, inflammatory biomarkers, and principal findings. The table provides a comparative overview of the clinical evidence and highlights variations in intervention protocols and reported inflammatory responses across the included studies.

Effects on Other Inflammatory Biomarkers

In addition to CRP, hs-CRP, IL-6, and TNF- α , several included studies evaluated a range of secondary inflammatory and oxidative stress biomarkers to provide a broader understanding of the anti-inflammatory potential of curcumin supplementation. These biomarkers included interleukin-1 beta (IL-1 β), interleukin-8 (IL-8), monocyte chemoattractant protein-1 (MCP-1), nuclear factor kappa B (NF- κ B), erythrocyte sedimentation rate (ESR), malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPx), and total antioxidant capacity (TAC). Although these biomarkers were assessed less frequently than CRP or IL-6, they provided valuable insights into the molecular mechanisms underlying the anti-inflammatory effects of curcumin.

The findings across the included studies demonstrated considerable diversity in the selection of biomarkers, reflecting differences in disease characteristics and study objectives. While inflammatory cytokines primarily represented systemic inflammatory responses, oxidative stress markers were commonly investigated to determine whether curcumin simultaneously reduced oxidative damage and enhanced endogenous antioxidant defense systems. This integrated assessment contributes to a more comprehensive evaluation of curcumin supplementation beyond conventional inflammatory biomarkers.

Table 5. Summary of Additional Biomarkers Evaluated Across Included Studies

Biomarker	Clinical Relevance	Typical Outcome Reported	Interpretation
IL-1 β	Pro-inflammatory cytokine	Change after intervention	Indicates modulation of inflammatory signaling
IL-8	Chemokine involved in leukocyte recruitment	Change after intervention	Reflects inflammatory cell activation
MCP-1	Monocyte recruitment marker	Change after intervention	Indicates immune cell migration
NF- κ B	Transcription factor	Activation or inhibition	Represents regulation of inflammatory pathways

ESR	General inflammatory marker	Reduction or no change	Indicates systemic inflammatory status
MDA	Oxidative stress marker	Reduction	Suggests decreased lipid peroxidation
SOD	Antioxidant enzyme	Increased activity	Indicates improved antioxidant defense
GPx	Antioxidant enzyme	Increased activity	Reflects enhanced oxidative protection
TAC	Total antioxidant capacity	Increased value	Demonstrates improved antioxidant status

Source: Authors' synthesis of inflammatory biomarkers discussed in the included studies and relevant literature.

Effects According to Disease Category

To facilitate clinical interpretation, the included studies were categorized according to disease conditions. Grouping studies by disease category enables comparison of curcumin supplementation across different inflammatory disorders and allows identification of clinical populations in which the intervention has been most extensively investigated.

Table 6. Data Extraction Framework According to Disease Category

Disease Category	Representative Population	Frequently Evaluated Biomarkers	Intervention Characteristics
Type 2 Diabetes Mellitus	Adults with T2DM	CRP, hs-CRP, IL-6	Oral curcumin supplementation
Obesity	Overweight and obese adults	hs-CRP, IL-6, TNF- α	Conventional or enhanced formulations
Metabolic Syndrome	Adults with metabolic syndrome	CRP, TNF- α	Various daily doses
Osteoarthritis	Patients with knee or hip osteoarthritis	CRP, TNF- α	Curcumin extract or phytosome
Rheumatoid Arthritis	Adults with autoimmune arthritis	CRP, IL-6	Oral supplementation
NAFLD	Adults with fatty liver disease	IL-6, TNF- α	Nano-curcumin or conventional formulations
Chronic Kidney Disease	CKD patients	CRP, IL-1 β	Curcumin supplementation
Other Chronic Diseases	Various clinical populations	Multiple inflammatory biomarkers	Study-specific interventions

Source: Authors' categorization of the included studies according to disease category, population, biomarkers, and intervention characteristics

Effects According to Curcumin Dosage

Daily curcumin dosage varied substantially among the included randomized controlled trials. Differences in dosage may influence therapeutic efficacy because curcumin exhibits limited oral bioavailability. Consequently, several studies

evaluated enhanced formulations designed to improve systemic absorption while maintaining relatively moderate daily doses.

Table 7. Data Extraction Framework According to Daily Curcumin Dose

Daily Dose Category	Common Formulations	Typical Intervention Duration	Biomarkers Commonly Evaluated
≤500 mg/day	Conventional curcumin	4–12 weeks	CRP, hs-CRP
501–1000 mg/day	Curcumin extract	8–16 weeks	CRP, IL-6, TNF-α
1001–1500 mg/day	Phytosomal curcumin	8–24 weeks	CRP, IL-6
>1500 mg/day	Nano-curcumin or liposomal formulations	8–24 weeks	Multiple inflammatory biomarkers

Source: Authors' synthesis of dosage categories and intervention characteristics reported in the included studies.

Effects According to Intervention Duration

Intervention duration is another important determinant of therapeutic response. The included studies evaluated supplementation periods ranging from several weeks to several months, allowing comparison of both short-term and longer-term interventions.

Table 8. Data Extraction Framework According to Intervention Duration

Duration	Description	Common Outcomes Evaluated
4 weeks	Short-term supplementation	Initial biomarker response
8 weeks	Intermediate intervention	CRP, IL-6, TNF-α
12 weeks	Standard clinical intervention	Multiple inflammatory biomarkers
16–24 weeks	Longer-term supplementation	Sustained inflammatory and oxidative stress responses

Source: Authors' synthesis of intervention-duration categories and outcomes reported in the included studies.

Risk of Bias Assessment

Methodological quality was evaluated using the Cochrane Risk of Bias Version 2 (RoB 2) framework. Five methodological domains were assessed, including the randomization process, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting. The assessment provides an overview of the internal validity of the included studies and supports interpretation of the certainty of evidence presented in this review.

Table 9. Risk of Bias Assessment of Included Randomized Controlled Trials

Risk of Bias Domains	Low Risk, n (%)	Some Concerns, n (%)	High Risk, n (%)	Total
D1. Randomization process	18 (66.7%)	7 (25.9%)	2 (7.4%)	27
D2. Deviations from intended interventions	20 (74.1%)	5 (18.5%)	1 (3.7%)	26

D3. Missing outcome data	21 (77.8%)	4 (14.8%)	2 (7.4%)	27
D4. Measurement of the outcome	19 (70.4%)	6 (22.2%)	2 (7.4%)	27
D5. Selection of the reported result	22 (81.5%)	4 (14.8%)	1 (3.7%)	27
Overall risk of bias	17 (63.0%)	8 (29.6%)	2 (7.4%)	27

Source: Authors' assessment based on the Cochrane Risk of Bias 2 tool (Sterne et al., 2019).

The methodological quality of the included randomized controlled trials was assessed using the Cochrane Risk of Bias 2 (RoB 2) tool. The assessment covered five domains, including the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. The overall risk-of-bias judgments were subsequently summarized to provide an overview of the methodological reliability of the included evidence.

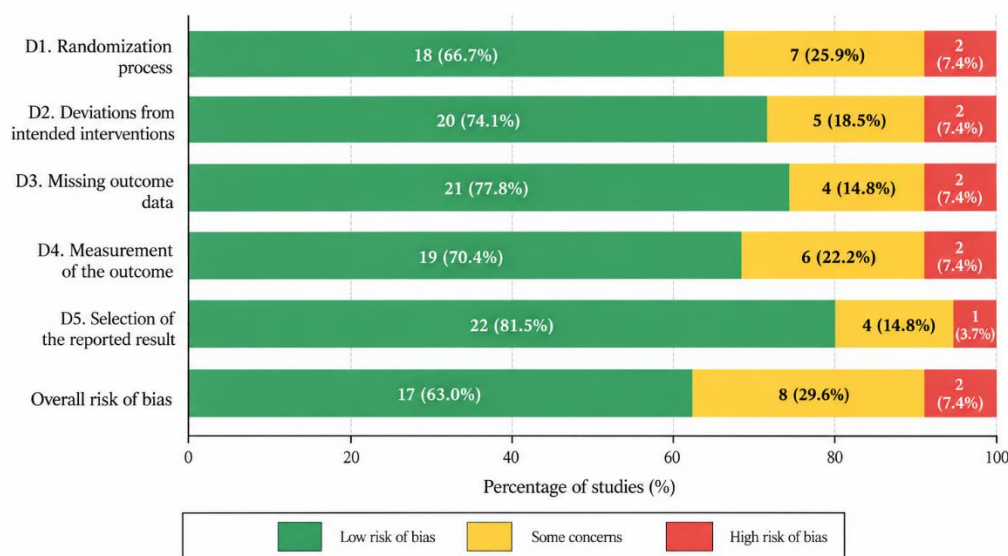


Figure 5. Risk of Bias Assessment of Included Randomized Controlled Trials

Source: Authors' assessment using the Cochrane Risk of Bias 2 (RoB 2) tool.

The risk-of-bias assessment provides a structured overview of methodological limitations across the included trials. The domain-level evaluation allows the identification of potential concerns related to randomization, intervention implementation, outcome measurement, and selective reporting. These methodological considerations were taken into account when interpreting the findings on curcumin supplementation and inflammatory biomarkers.

Interpretation of Anti-Inflammatory Effects and Clinical Implications

Based on the results of this systematic review, curcumin supplementation can be associated to the modulation of systemic inflammation, mainly by influencing the levels of CRP, hs-CRP, IL-6 and TNF- α . This indicates that curcumin can modulate inflammatory response from the acute-phase protein and cytokine levels. The consistent results from multiple biomarkers are biologically significant since chronic inflammation involves a multi-step process involving multiple interconnected signaling pathways rather than any single inflammatory mediator. The findings are generally consistent with the previous evidence syntheses, which reported increases in reducing CRP, IL-6, and TNF- α with curcumin supplementation (Naghsh et al., 2023; Dehzad et al., 2023; Kavyani et al., 2024).

However, the results cannot be presumed to be equally effective. Variations in disease conditions, baseline inflammatory status, dosage, duration of intervention and formulation could account for the differences in treatment response. There was also significant heterogeneity in previous meta-analyses, with similar findings for CRP and IL-6, and some analyses indicating that IL-1 β did not appear to be significantly affected (Naghsh et al., 2023; Dehzad et al., 2023).

This is significant because although statistical changes in biomarkers may be favorable, they may not be the same in different patient groups. Bioavailability enhanced formulations are also highlighted in the review. Conventional curcumin is not very bioavailable orally, while phospholipid complexes, liposomal and piperine enhanced curcumin formulations have been proposed to ensure higher bioavailability. This explains some variation in effectiveness of interventions, but currently there is no evidence to suggest one formulation is consistently better. In theory, the results contribute to the knowledge of the nutritional anti-inflammatory therapeutic opportunities by linking formulation properties, exposure to the treatment, and response of biomarkers in an integrated manner.

In practice, curcumin can be used as an adjunct nutritional measure, but not as a substitute for existing therapeutic modalities. Its potential application should take into account the disease-specific conditions, formulation, dosage, and clinical supervision. This review is novel because it considers multiple inflammatory markers, as well as the characteristics of the interventions, in a single comprehensive review in multiple adult populations, not just a single biomarker or single disease category.

There are a number of restrictions to consider. There is clinical and methodological heterogeneity, outcome measure differences, fairly short intervention periods, and small sample sizes, which limit direct comparisons. Moreover, the narrative synthesis does not produce pooled causal effect estimates or specific causal dose-response relationships. Larger randomized trials with standardized curcumin product and uniform measurement of biomarkers, longer follow-up, and clinically significant endpoints should be the focus of future research. Whether baseline inflammation, disease characteristics and formulation are explanatory of treatment variability should also be explored in dose-response analyses and in subgroup investigations.

CONCLUSION

This systematic review synthesized the current evidence regarding the effects of curcumin supplementation on inflammatory biomarkers across diverse clinical populations. Overall, the reviewed literature suggests that curcumin has promising anti-inflammatory properties, with the most consistent improvements observed in commonly assessed biomarkers such as C-reactive protein, high-sensitivity C-reactive protein, interleukin-6, and tumor necrosis factor alpha. Although the magnitude of the therapeutic response varied among studies, differences were largely attributable to participant characteristics, baseline inflammatory status, intervention duration, dosage, and the formulation used to enhance curcumin bioavailability. These findings reinforce the potential role of curcumin as a complementary nutritional strategy for managing chronic inflammation associated with metabolic, autoimmune, musculoskeletal, and other chronic diseases.

From a theoretical perspective, this review strengthens the understanding of the multifactorial mechanisms through which curcumin modulates inflammatory pathways and oxidative stress. Practically, the findings support consideration of curcumin supplementation as an adjunctive intervention within evidence-based clinical and nutritional management, while emphasizing the importance of selecting appropriate formulations and treatment protocols. Nevertheless, the available

evidence remains limited by methodological heterogeneity, relatively small sample sizes, short intervention periods, and variations in outcome measurements across studies. Future research should prioritize large-scale, multicenter randomized controlled trials using standardized dosages, intervention durations, and biomarker panels to improve comparability and strengthen the certainty of clinical evidence.

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