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Curcumin as a Nutraceutical Candidate in Cancer: A Systematic Review of Preclinical Antiproliferative, Anti-Metastatic, and Formulation Evidence

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ABSTRACT

Curcumin, a polyphenolic constituent of turmeric (*Curcuma longa*), has been investigated as a food-derived nutraceutical with potential anticancer properties, but its clinical translation is limited by poor aqueous solubility, chemical instability, rapid metabolism, and low systemic exposure. This systematic review, conducted following PRISMA 2020, synthesized preclinical evidence on the antiproliferative, anti-metastatic, and formulation-related effects of native curcumin and curcumin-containing formulations in cancer models. A systematic search of PubMed/MEDLINE, Scopus, ScienceDirect, and SpringerLink (January 2016 to 20 June 2026) identified 15 eligible studies: nine on native curcumin and six on curcumin formulations. Across multiple cancer models, including breast, ovarian, colorectal, thyroid, pancreatic, hepatocellular, and meningioma, curcumin generally reduced cancer-cell viability, proliferation, migration, invasion, epithelial-mesenchymal transition, and tumor growth, with effects converging on signaling pathways involved in cell survival, inflammation, and metastatic behavior. Evidence was predominantly in vitro, with limited animal-model confirmation. Formulation studies demonstrated measurable improvements over native curcumin: an ionic-liquid system increased aqueous solubility by approximately 8,750-fold and reduced MDA-MB-231 viability by about 60% at 10 micrograms per milliliter without comparable toxicity in normal fibroblasts; curcumin nanocapsules showed a lower IC50 than microcapsules in breast cancer cells; and spanlastics produced stronger anticancer activity than nanocrystals, which instead showed the most rapid dissolution. Overall, curcumin demonstrates promising preclinical bioactivity, but evidence remains limited by substantial heterogeneity in models, formulations, doses, exposure durations, and outcome measures, preventing meta-analysis. These findings support curcumin as a biologically active nutraceutical candidate requiring further pharmacokinetic, safety, and in vivo validation before translational application in cancer care.

INTRODUCTION

Cancer progression is characterized by uncontrolled cellular proliferation and the acquisition of invasive and metastatic phenotypes. Metastatic progression involves several interrelated biological processes, including epithelial–mesenchymal transition (EMT), extracellular-matrix remodeling, migration, invasion, angiogenesis, and survival of tumor cells in secondary tissue environments. These processes are influenced by multiple interacting molecular pathways, indicating that cancer progression cannot be explained by a single signaling mechanism. This has encouraged growing

interest in multi-target bioactive compounds, particularly those capable of affecting both tumor-cell proliferation and metastasis-related processes.[6,10,16]

Curcumin is the main bioactive polyphenol found in turmeric (*Curcuma longa*), which is commonly used as a culinary spice and traditional medicinal ingredient. However, in preclinical cancer research, curcumin is usually studied as a purified nutraceutical compound or as a formulated pharmacological agent. Therefore, the anticancer effects observed in experimental studies should not be directly equated with the effects of regular dietary intake of turmeric.[7,21]

Curcumin remains highly relevant in cancer nutraceutical research because it continues to be widely investigated in preclinical oncology, particularly through formulation-based approaches designed to improve its delivery and biological activity. Preclinical studies suggest that curcumin may influence several key processes in cancer development, including tumor-cell growth, apoptosis, inflammation, angiogenesis, migration, invasion, and metastasis. These effects are generally associated with signaling pathways involved in cell survival, inflammatory regulation, EMT, and extracellular-matrix degradation, including PI3K/Akt, NF-κB, TGF-β/Smad, and MMP-related pathways. Since these mechanisms are closely connected, the effect of curcumin may vary across cancer types, formulations, doses, exposure times, and experimental models.[13,22–24]

Despite its promising biological activity, the clinical translation of curcumin remains limited by poor aqueous solubility, instability under physiological conditions, limited gastrointestinal absorption, rapid metabolism, and low systemic exposure. [7] These limitations create a gap between the anticancer effects observed in vitro and their possible relevance in vivo or clinically. In particular, curcumin concentrations that suppress cancer-cell proliferation, migration, invasion, or other metastasis-related behaviors in experimental models may not be achievable through regular dietary turmeric intake or conventional curcumin supplementation.

To address these limitations, various curcumin formulation strategies have been developed, including nanoparticles, liposomes, micelles, vesicular systems, polymeric carriers, nanocrystals, and other solubilization platforms. These systems are designed to improve curcumin solubility, stability, controlled release, cellular delivery, and biological activity.[15] However, improved physicochemical properties or cellular uptake should not automatically be interpreted as evidence of improved systemic bioavailability or clinical effectiveness unless supported by pharmacokinetic, tissue-distribution, or in vivo efficacy data.

Previous narrative reviews have summarized curcumin's broader pharmacological profile and delivery technologies. Naksuriya et al.[15] reviewed nano-sized curcumin delivery systems—including liposomes, polymeric nanoparticles, micelles, conjugates, and lipid nanoparticles—alongside efficacy data from cell-line, in vivo, and clinical studies across multiple disease contexts. Tomeh et al.[22]

summarized the medicinal chemistry, pharmacology, and mechanisms of curcumin and its derivatives as anticancer agents, drawing on experimental, animal, and human data, and briefly noted advances in drug-delivery systems. However, both reviews were narrative rather than systematic in design, without a predefined protocol, systematic search strategy, or risk-of-bias appraisal, and neither presented an integrated framework linking formulation-related physicochemical improvements to specific antiproliferative and anti-metastatic signaling outcomes in cancer models. Furthermore, neither review consistently distinguished turmeric as a dietary source, curcumin as an isolated nutraceutical compound, and formulated curcumin as a pharmacologically engineered agent—a distinction that is central to interpreting translational relevance.

Therefore, the main gap addressed in this systematic review is the lack of an integrated synthesis—grounded in a clear distinction between curcumin as a nutraceutical compound and as a formulated pharmacological agent—explaining how curcumin formulation characteristics may influence cellular delivery and subsequently affect antiproliferative and anti-metastatic outcomes in preclinical cancer models.

MATERIALS AND METHODS

Study Design

A systematic review was conducted and reported in accordance with the PRISMA 2020[18] statement to evaluate the antiproliferative, anti-metastatic, and formulation-related effects of native and formulated curcumin in preclinical cancer models. This review was designed prospectively in accordance with PRISMA principles. The protocol has been submitted for registration in PROSPERO and is currently pending approval; the registration number will be provided upon acceptance.

Eligibility Criteria

Studies were included if they were original full-text articles evaluating native or formulated curcumin in cancer cell lines, 3D models, tumor-bearing animal models, or clinically derived cancer materials, and reported at least one relevant biological or physicochemical outcome. Studies were excluded if they involved synthetic curcumin analogs, undefined turmeric extracts, non-cancer outcomes, or multi-phytochemical combinations in which curcumin's contribution could not be distinguished. For the purposes of this review, anti-metastatic evidence was defined broadly as outcomes related to cancer-cell migration, invasion, epithelial–mesenchymal transition, matrix metalloproteinase expression, and distant-organ metastasis. Because distant-organ metastasis was evaluated in only a limited number of studies, most evidence represented metastasis-related phenotypes rather than direct demonstration of metastatic suppression.

Search Strategy

A systematic literature search was conducted in PubMed/MEDLINE, Scopus, ScienceDirect, and SpringerLink for articles published from January 2016 to 20 June 2026. The literature search and its reporting were guided by the PRISMA-S extension.[19] The search strategy combined terms related to curcumin, cancer, antiproliferative activity, metastatic phenotypes, and formulation characteristics using the Boolean operators “AND” and “OR.”

The core search strategy was: (“curcumin” OR “nanocurcumin” OR “nano-curcumin” OR “curcumin nanoparticle*” OR “curcumin formulation*” OR “curcumin micelle*” OR “curcumin niosome*” OR “curcumin nanocrystal*” OR “curcumin capsule*” OR “curcumin-loaded”) AND (cancer OR carcinoma OR tumor OR neoplasm* OR malignan*) AND (proliferat* OR viability OR cytotoxicity OR apoptosis OR “cell cycle” OR “colony formation” OR migration OR invasion OR metastas* OR EMT OR “epithelial-mesenchymal transition” OR “matrix metalloproteinase*” OR MMP-2 OR MMP-9 OR solubility OR dissolution OR stability OR encapsulation OR “drug loading” OR “drug release” OR “cellular uptake” OR “drug delivery”).

The search syntax was adapted to the requirements of each database. Reference lists of eligible studies and relevant reviews were also screened to identify additional publications.

Study Selection and Data Extraction

All identified records were imported into Parsifal, and duplicate records were removed before screening. Study selection involved tittle and abstract screening followed by full-text assessment against the eligibility criteria. Screening was performed by one reviewer and verified by a second reviewer. Disagreements were resolved through discussion or consultation of a third reviewer when consensus could not be reached.

A standardized data-extraction form was used to collect information on author and year, cancer type, experimental model, curcumin form, formulation or carrier material, dose, exposure duration, comparator, assay method, antiproliferative outcomes, anti-metastatic outcomes, molecular pathways, physicochemical characteristics, safety findings, and major study limitations. The study-selection process was documented using a PRISMA 2020 flow diagram[18].

Data Synthesis and Quality Assesment

Meta-analysis was not performed due to substantial heterogeneity across studies. Findings were narratively synthesized and categorized into: antiproliferative effects, anti-metastatic effects, molecular pathways, physicochemical outcomes, comparative formulation performance, and safety or in vivo evidence.

Risk of bias and reporting reliability were evaluated using a modified preclinical assessment framework informed by SYRCLE’s risk-of-bias guidelines[8] for animal studies and ToxRTool-style reliability principles[20] for in vitro mechanistic studies. These frameworks were used to guide the

selection of appraisal domains, but were not applied as standalone numerical scoring instruments. Seven domains were assessed: clarity of controls, dose-response reporting, replication, blinding or bias control, outcome measurement, reporting completeness, and mechanistic support. Each domain was judged as low concern, some concern, or high concern. The overall judgment for each study was determined narratively based on the number and severity of concerns across domains.

Formal certainty-of-evidence grading (e.g., GRADE) was not performed, as this framework is primarily designed for clinical intervention studies with comparable outcome measures and is not well suited to heterogeneous preclinical models with divergent cell lines, assays, and endpoints. Instead, methodological confidence was appraised narratively through the seven-domain risk-of-bias framework described above.

RESULTS

Study selection

A total of 1,337 records were identified through searches of four databases, comprising 4 records from PubMed, 923 from ScienceDirect, 284 from Scopus, and 126 from SpringerLink. After the removal of 40 duplicate records, 1,297 records were screened based on their titles and abstracts. Of these, 1,205 records were excluded, and 92 reports were sought for full-text retrieval. Thirteen reports could not be retrieved; therefore, 79 full-text articles were assessed for eligibility. Following the exclusion of 64 articles that did not meet the predefined eligibility criteria, 15 studies were included in the final narrative synthesis. The study-selection process is presented in the PRISMA 2020 flow diagram in Figure 1.

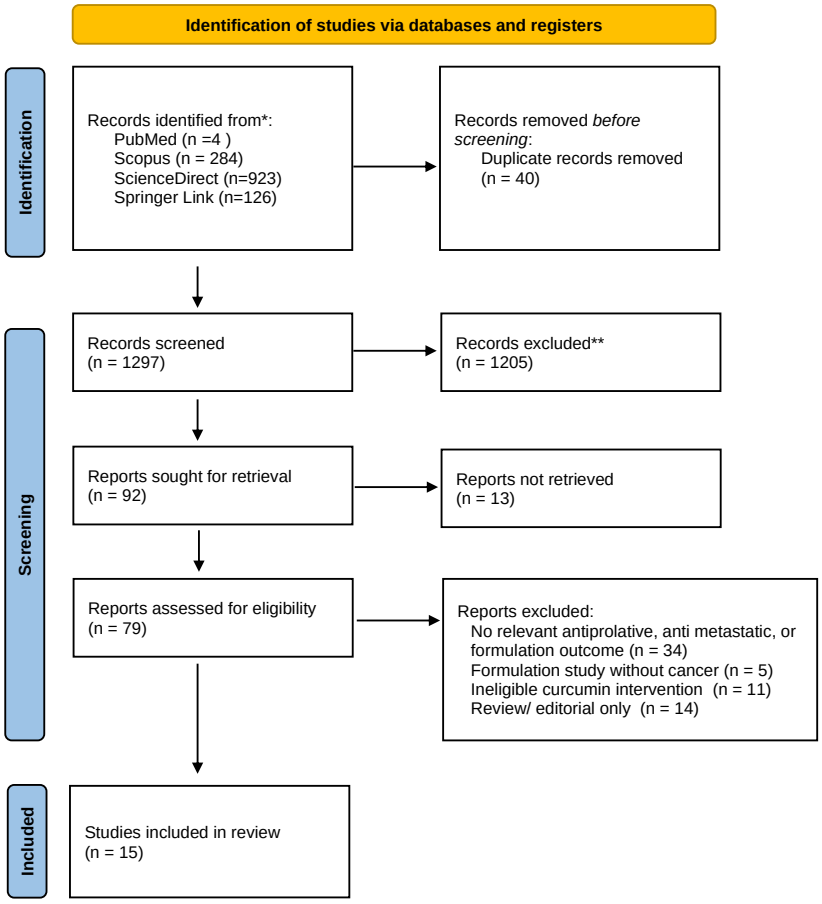

Figure 1. PRISMA 2020 flow diagram of the study-selection process[18]

Study characteristics

The 15 included studies were published between 2016 and 2026. Nine studies evaluated native curcumin, either alone or in mechanistically interpretable combination with standard treatment or signaling stimulation, whereas six studies evaluated curcumin formulations. The evidence was dominated by in-vitro experiments, although several studies incorporated xenograft or tumor-bearing animal models. Cancer models included breast, ovarian, colorectal, papillary thyroid, pancreatic, hepatocellular, and malignant meningioma models.

Table 1. Characteristics and principal findings of studies evaluating native curcumin

Study	Cancer model and study design	Intervention	Main outcomes	Molecular pathway	Principal finding
Hu et al., 2019	Breast cancer; in vitro	Native curcumin	Cell viability, stemness, migration, invasion, and EMT	Stemness- and EMT-related signaling	Curcumin reduced stem-like properties, migration, invasion, and the mesenchymal phenotype.
Zhang et al., 2016	Papillary thyroid cancer; in vitro	Native curcumin	Migration, invasion, EMT, MMP-2, and MMP-9	TGF-β/Smad2/3	Curcumin suppressed migration, invasion, EMT, and MMP expression through inhibition of TGF-β/Smad2/3 signaling.
Li et al., 2022	Triple-negative breast cancer; in vitro	Native curcumin	Proliferation, migration, invasion, EMT, and stemness	Hedgehog/Gli1	Curcumin inhibited proliferation, invasive behavior, EMT, and stemness-related characteristics.
Zhao et al., 2022	Hepatocellular carcinoma; in vitro and in vivo	Native curcumin	Proliferation, migration, invasion, tumor growth, and lung metastasis	Bclaf1/Wnt/β-catenin	Curcumin suppressed tumor progression and lung metastasis through Bclaf1-mediated Wnt/β-catenin regulation.
Cao et al., 2016	Pancreatic cancer under hypoxic conditions; in vitro	Native curcumin	Migration, invasion, and EMT	Hedgehog/SHH/SMO/ GLI1	Curcumin inhibited hypoxia-induced migration, invasion, and EMT and restored epithelial characteristics.
Liang et al., 2021	Papillary thyroid cancer; in vitro	Native curcumin	Cell viability, migration, invasion, EMT, MMP-2, and MMP-9	miR-301a-3p/STAT3	Curcumin reduced viability and invasive phenotypes through regulation of the miR-301a-3p/STAT3 axis.
Yu et al., 2025	Colorectal cancer; in vitro and in vivo	Native curcumin	Proliferation, migration, and tumor growth	TRIM2/Akt/mTOR	Curcumin downregulated TRIM2 and suppressed Akt/mTOR/S6K/4EBP1 signaling, proliferation, migration, and tumor growth.
Yin et al., 2019	Oxaliplatin-resistant colorectal cancer; in vitro and in vivo	Curcumin alone and combined with oxaliplatin	Proliferation, apoptosis, invasion, EMT, and xenograft response	TGF-β/Smad2/3	Curcumin reduced oxaliplatin resistance and EMT and enhanced treatment response through TGF-β/Smad2/3 inhibition.
Chen et al., 2021	Malignant meningioma; in vitro and xenograft model	Curcumin in an HGF-stimulated model	Proliferation, migration, invasion, EMT, and tumor growth	HGF/c-MET/PI3K/Akt/mTOR	Curcumin inhibited HGF-induced proliferation, migration, invasion, EMT, and xenograft growth.

Table 2. Characteristics, physicochemical outcomes, and anticancer findings of curcumin formulation studies

Study	Cancer model and study design	Curcumin formulation	Formulation-related outcomes	Biological outcomes	Principal finding
Liu et al., 2024	Ovarian cancer; in vitro	Curcumin nanoparticles	Cellular uptake and nanoparticle-mediated delivery	Proliferation, migration, and EMT	Curcumin nanoparticles produced stronger antiproliferative and anti-migratory effects than free curcumin through NF-κB/PRL-3 modulation.
Bahreyni Toossi et al., 2026	Colorectal cancer and normal fibroblasts; in vitro	Bulk curcumin, curcumin nanomicelles, and	Comparative nanoformulation performance	Viability, apoptosis, clonogenic survival, radiosensitization, and radioprotection	The biological effects varied by formulation, with nanomicelles showing radiosensitizing activity in cancer cells and relative protective effects in normal cells.

		curcumin nanoniosomes			
Moawad et al., 2026	Breast cancer; in vitro	Curcumin microcapsules and nanocapsules	Micro- versus nanoencapsulation	Viability, cell cycle, apoptosis, Ki-67, C-Myc, EGFR, and VEGFR2	Curcumin nanocapsules showed a lower IC_{50} and stronger antiproliferative and pro-apoptotic activity than microcapsules.
Özerkan et al., 2026	Colorectal cancer; 2D and 3D models	NIR-sensitive curcumin-loaded gelatin nanoparticles	Particle characterization and NIR-triggered release	Viability, migration, invasion, apoptosis, mitochondrial effects, and selectivity	NIR activation accelerated curcumin release and enhanced antiproliferative, anti-migratory, and anti-invasive activity.
Almutairi et al., 2026	Breast cancer; in vitro	Free curcumin, curcumin spanlastics, and curcumin nanocrystals	Particle characteristics, entrapment, stability, and dissolution	Viability, apoptosis, Cyclin D1, VEGF, NF-κB, and PI3K/Akt/mTOR	Spanlastics showed the strongest anticancer activity, whereas nanocrystals demonstrated the most rapid dissolution.
Bisht et al., 2026	Triple-negative breast cancer and normal fibroblasts; in vitro	Curcumin dissolved in a superbase ionic liquid	Aqueous solubility and chemical stability	Cancer-cell viability and normal-cell compatibility	The ionic-liquid system increased curcumin solubility by approximately 8,750-fold, prolonged stability, and selectively reduced cancer-cell viability.

Risk Of Bias and Methodological Qualilty Assessment

The methodological quality of the included studies was generally acceptable, although several reporting limitations were identified. Most studies provided clear experimental controls, relevant outcome measurements, and sufficient biological or mechanistic endpoints. The main recurring concern was the limited reporting of blinding, randomization, or other bias-control procedures, particularly in studies involving image-based assays, migration or invasion assessment, and animal or xenograft models. Several studies also did not clearly distinguish between technical and biological replication. Overall, no study was judged as having high methodological concern across all domains. Most studies were categorized as having low-to-moderate or moderate concern, mainly due to incomplete reporting of blinding, randomization, or replication details.

Table 3. Risk of Bias and Methodological Quality Assessment of Included Studies

Study	Controls	Dose-response	Replication	Blinding/bias control	Outcome measurement	Reporting completeness	Mechanistic support	Overall concern
Yin 2019	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — in vitro and in vivo outcomes reported	Strong — TGF-β/Smad2/3, EMT, apoptosis, and xenograft response	Low-moderate
Yu 2025	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — proliferation, migration, gene expression, IHC, and animal data reported	Strong — TRIM2 knockdown, mTOR pathway, and rescue experiment	Low-moderate
Liu 2024	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — uptake, proliferation, migration, EMT, and inflammatory markers reported	Moderate-high — NF-κB/PRL-3 pathway with LPS and p65 overexpression	Moderate
Almutairi 2026	Adequate	Adequate	Reported	Unclear in most assays	Adequate	Adequate — formulation, viability, apoptosis, and ELISA markers reported	Strong — PI3K/AKT/mTOR, NF-κB, Cyclin D1, VEGF, BAX, P53, and Bcl-2	Low-moderate
Bisht 2026	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — solubility, stability, cancer-cell viability, and normal-cell compatibility reported	Limited-moderate — mainly solubility and functional anticancer evidence	Moderate
Özerkan 2026	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — 2D/3D model, viability, migration, invasion, apoptosis, and selectivity reported	Moderate — apoptosis, mitochondrial damage, and IR-triggered delivery reported	Moderate
Zhang 2016	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — migration, invasion, EMT, MMP-2/MMP-9, and Smad phosphorylation reported	Strong — TGF-β/Smad2/3 pathway and EMT/MMP markers confirmed	Low-moderate

Study	Controls	Dose-response	Replication	Blinding/bias control	Outcome measurement	Reporting completeness	Mechanistic support	Overall concern
Hu 2019	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — proliferation, stemness, EMT, migration, and invasion reported	Moderate — stemness and EMT markers reported, but no rescue experiment	Moderate
Li 2022	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — proliferation, invasion, migration, stemness, EMT, and xenograft-related data reported	Strong — Hedgehog/Gli1 pathway, Gli1 overexpression, EMT, and stemness markers	Low-moderate
Zhao 2022	Adequate	Reported/likely	Reported/likely	Unclear in most assays	Adequate	Adequate — migration, invasion, tumor growth, and lung metastasis reported	Strong — Bclaf1-mediated Wnt/β-catenin pathway and metastasis evidence	Low-moderate
Cao 2016	Adequate	Reported/likely	Reported/likely	Unclear in most assays	Adequate	Adequate — proliferation, migration, invasion, EMT, and Hh pathway markers reported	Moderate-high — Hh/SHH/SMO/GLI1 and EMT markers assessed, but no rescue experiment	Moderate
Liang 2021	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — viability, migration, invasion, MMPs, EMT, and JAK/STAT markers reported	Strong — miR-301a-3p/STAT3 axis tested with mimics, inhibitors, and STAT3 overexpression	Low-moderate
Chen 2021	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — proliferation, migration, invasion, EMT, and tumor growth reported	Strong — c-MET/PI3K/Akt/mTOR pathway supported by inhibitor experiments	Low-moderate
Moawad 2026	Adequate	Adequate	Reported	Unclear in most assays	Adequate	Adequate — viability, apoptosis, cell cycle, gene expression, and bioinformatics reported	Moderate-high — EGFR, VEGFR2, C-myc, Ki-67, Caspase-3, and pathway enrichment reported	Low-moderate

Study	Controls	Dose-response	Replication	Blinding/bias control	Outcome measurement	Reporting completeness	Mechanistic support	Overall concern
Bahreyni Toossi 2026	Adequate	Adequate	Reported/likely	Unclear in most assays	Adequate	Adequate — viability, apoptosis, clonogenic survival, cancer and normal cells reported	Limited-moderate — radiosensitizing/radioprotective outcomes strong, but pathway data limited	Moderate

Direction of evidence map

A semi-quantitative direction-of-effect analysis was conducted to summarize the consistency of supportive findings across the included studies. Overall, the direction of evidence was favorable for curcumin across the main biological outcomes. Antiproliferative effects were reported in most native curcumin studies and all curcumin formulation studies. Native curcumin studies more consistently reported inhibition of migration or invasion, EMT/MMP suppression, molecular pathway modulation, and in vivo or tumor-related effects. In contrast, formulation studies primarily supported improved anticancer activity in vitro, while evidence for anti-metastatic phenotypes and in vivo tumor outcomes was less frequently reported. This pattern suggests that native curcumin studies were more focused on mechanistic and anti-metastatic endpoints, whereas formulation studies mainly emphasized enhanced delivery, solubility, stability, and cytotoxic potency.

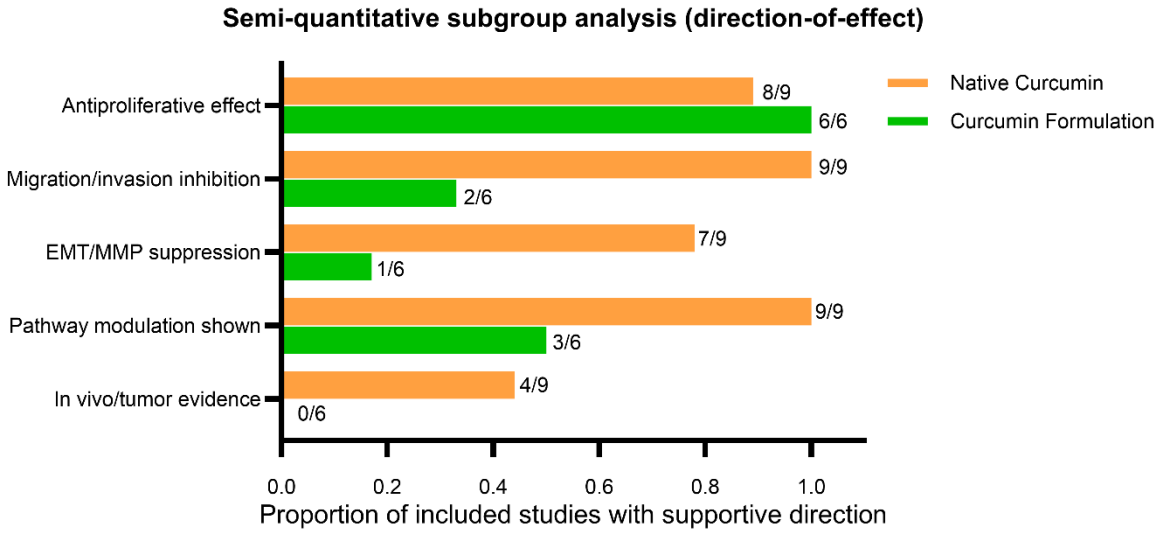

Figure 2. Semi-quantitative direction-of-effect analysis of native curcumin and curcumin formulation studies. The graph shows the proportion of included studies reporting a supportive direction of effect for each outcome category. Values are presented as n/N. This analysis summarizes the direction of evidence only and does not represent a pooled effect size or meta-analysis.

Antiproliferative effects

Across studies of native curcumin, treatment generally reduced cell viability, proliferation, colony formation, and tumor growth, with several studies reporting concentration- and/or time-dependent effects.[4,5,9,11,12,23–26] These effects were associated with the suppression of proliferative, survival, and stemness-related regulators, including Akt/mTOR, S6K, 4EBP1, Cyclin D1, Ki-67, C-Myc, EGFR, VEGFR2, and cancer stem-cell-associated factors.[1,9,11,14,24] Apoptosis was promoted through increased caspase activity and pro-apoptotic signaling, accompanied by reduced expression of anti-apoptotic proteins in several cancer models.[1,2,5,14,17,23]

Formulation studies generally reported improved anticancer potency or more rapid biological effects compared with free curcumin.[1–3,13,14,17] Curcumin nanocapsules produced a lower IC_{50} than microcapsules in MCF-7 cells, whereas spanlastics showed stronger suppression of proliferation- and survival-related pathways than native curcumin or nanocrystals.[1,14] The curcumin/SBIL formulation reduced MDA-MB-231 cell viability by approximately 60% at 10 µg/mL after 24 hours without producing comparable toxicity in L929 fibroblasts.[3] These findings indicate that formulation strategies may alter effective intracellular exposure and biological activity. However, direct comparisons between studies remain limited because of differences in cancer models, dose units, treatment duration, and outcome measurements.

Anti-migratory, anti-invasive, and EMT-modulating effects

Curcumin reduced migration and/or invasion across breast, thyroid, pancreatic, hepatocellular, colorectal, ovarian, and meningioma models. [4,5,9,11–13,23–26] These effects were frequently accompanied by restoration of epithelial characteristics, particularly increased E-cadherin expression, and suppression of mesenchymal markers such as N-cadherin, vimentin, and fibronectin.[4,5,9,11–13,23,25] Several studies also reported reduced expression or activity of MMP-2 and MMP-9, providing a plausible mechanism for decreased extracellular-matrix degradation and cellular invasion.[12,25]

The strongest translational evidence was provided by studies incorporating animal models. In hepatocellular carcinoma, curcumin suppressed tumor growth and lung metastasis through Bclaf1-mediated regulation of Wnt/β-catenin signaling.[26] In oxaliplatin-resistant colorectal cancer, curcumin attenuated EMT and improved treatment response in vivo through modulation of TGF-β/Smad2/3 signaling.[23] In malignant meningioma, curcumin reduced xenograft growth and HGF-induced EMT through inhibition of c-MET-dependent PI3K/Akt/mTOR signaling.[5] Nevertheless, distant-organ metastasis was directly evaluated in only a limited number of studies.

Molecular pathway convergence

Despite differences in cancer type and experimental design, the included studies converged on several interconnected signaling networks. TGF-β/Smad2/3 signaling mediated EMT and treatment resistance in thyroid and colorectal cancer models.[23,25] Hedgehog/Gli1 signaling was implicated in triple-negative breast and pancreatic cancer.[4,11] Wnt/β-catenin/Bclaf1 signaling regulated hepatocellular cancer invasion and metastasis.[26] NF-κB/PRL-3 contributed to ovarian cancer proliferation and migration[13], whereas the miR-301a-3p/STAT3 axis regulated papillary thyroid cancer viability, migration, and invasion.[12] TRIM2 acted upstream of Akt/mTOR signaling in colorectal cancer[24], while c-MET-dependent PI3K/Akt/mTOR signaling mediated HGF-induced proliferation, migration, invasion, and EMT in meningioma. [5]

Solubility, stability, dissolution, and release

The formulation studies directly addressed major physicochemical limitations of native curcumin. Spanlastics and nanocrystals increased dissolution efficiency compared with curcumin powder, with nanocrystals demonstrating rapid and near-complete release during the early dissolution period.[1] The SBIL formulation increased aqueous curcumin solubility from approximately 0.0004 mg/g to 3.5 mg/g and prolonged its estimated half-life to approximately 385 hours in the optimized aqueous solution.[3] NIR-sensitive gelatin nanoparticles enabled externally activated curcumin release, with infrared stimulation accelerating early drug release and enhancing anticancer activity.[17]

These findings demonstrate improvements in solubility, dissolution, chemical stability, and controlled release.[1,3,17] However, most formulation studies did not directly measure pharmacokinetic parameters such as plasma concentration, area under the curve, Cmax, Tmax, or tissue distribution.[1–3,13,14,17] Therefore, improved physicochemical performance should be interpreted as supporting the potential for improved bioavailability rather than as direct evidence of enhanced systemic bioavailability.

Formulation strategies, selectivity, and safety

The included formulation strategies were heterogeneous and comprised curcumin nanoparticles, nanomicelles, nanoniosomes, microcapsules, nanocapsules, gelatin nanoparticles, spanlastics, nanocrystals, and ionic-liquid-mediated solubilization systems.[1–3,13,14,17] Particle size, zeta potential, encapsulation efficiency, drug loading, dissolution, stability, release kinetics, cellular uptake, and normal-cell compatibility were reported inconsistently across studies.

Several studies included non-cancer cell controls. Curcumin nanomicelles showed differential radiosensitizing effects in HT-29 cancer cells and radioprotective effects in HFF cells, although some formulation-related toxicity was also reported.[2] NIR-activated Cur-GelNPs showed lower toxicity toward HUVECs than toward colorectal cancer cells.[17] Curcumin/SBIL remained cytocompatible with L929 fibroblasts at concentrations that substantially reduced MDA-MB-231 viability.[3] Although these findings suggest a degree of cancer-cell selectivity, they remain insufficient to establish clinical safety because long-term toxicity, biodistribution, metabolism, and interactions with conventional anticancer treatments were rarely evaluated.

DISCUSSION

Principal findings

This systematic review found that native curcumin and curcumin-containing formulations generally showed antiproliferative, anti-migratory, anti-invasive, EMT-modulating, and formulation-related benefits in preclinical cancer models. Native curcumin consistently suppressed cancer-cell

proliferation and metastatic phenotypes through coordinated regulation of multiple signaling pathways [4,5,9,11–13,23–26] while curcumin-containing formulations additionally improved one or more limiting physicochemical or delivery-related properties, including dissolution, chemical stability, controlled release, cellular uptake, and anticancer potency.[1–3,13,14,17] However, the direction and strength of these findings should be interpreted cautiously, as most included studies were based on in vitro models, used heterogeneous doses and exposure durations, and reported different biological endpoints. Collectively, the evidence supports curcumin as a biologically active food-derived nutraceutical candidate, but it does not establish curcumin as a clinically proven anticancer intervention.

Nevertheless, the included evidence was not fully consistent. The formulation type identified as most effective differed across studies depending on the specific comparator used—curcumin nanocapsules outperformed microcapsules in one study, whereas spanlastics outperformed nanocrystals in another—such that no single formulation platform was consistently superior across the literature. Similarly, although several studies reported cancer-cell-selective toxicity, at least one formulation study also noted measurable toxicity toward normal cells, indicating that selectivity was not uniform across delivery systems. These inconsistencies suggest that formulation superiority claims are comparator-dependent rather than generalizable.

Relationship between proliferation and metastasis

The antiproliferative and anti-metastatic effects of curcumin were frequently interrelated. Signaling pathways such as PI3K/Akt/mTOR, STAT3, NF-κB, Wnt/β-catenin, Hedgehog/Gli1, and TGF-β/Smad regulate both tumor-cell growth and invasive plasticity.[4,5,9,11–13,23–26] However, evidentiary support across these pathways was uneven: TGF-β/Smad2/3 and PI3K/Akt/mTOR signaling were corroborated by multiple studies with in vivo confirmation, whereas Hedgehog/Gli1, Wnt/β-catenin, NF-κB/PRL-3, STAT3, and TRIM2/mTOR involvement each rested on single-study evidence within this review and warrant more cautious interpretation. Curcumin-mediated inhibition of these pathways may therefore reduce proliferation while simultaneously limiting migration, invasion, epithelial–mesenchymal transition, extracellular-matrix degradation, and stemness-related characteristics. [4,5,9,11–13,23,24,26].

Nevertheless, migration and invasion findings should be interpreted carefully because reduced wound closure or Transwell movement may partly result from cytotoxicity or slower proliferation rather than a specific anti-migratory effect. Future studies should therefore use non-cytotoxic concentrations, matched proliferation controls, mitosis-adjusted migration methods, and time-lapse imaging to distinguish migration-specific effects from general growth inhibition.

Curcumin as a food-derived nutraceutical

The classification of curcumin as a food-derived nutraceutical is scientifically defensible because curcumin originates from turmeric, a widely consumed culinary spice, and exhibits biological effects beyond its basic nutritional role.[7,21] However, the studies included in this review predominantly used isolated curcumin or engineered curcumin formulations rather than turmeric-containing foods, dietary patterns, or conventional dietary exposure. [1–5,9,11–14,17,23–26]

The micromolar concentrations applied in cell-culture studies cannot be directly translated into dietary intake. Consequently, the findings do not demonstrate that ordinary turmeric consumption prevents cancer progression or metastasis. Curcumin should therefore be described as a food-derived nutraceutical candidate rather than an established nutritional therapy. Its future role may be more plausible as a standardized adjunct to conventional cancer treatment than as a substitute for surgery, chemotherapy, radiotherapy, targeted therapy, immunotherapy, or evidence-based medical nutrition therapy.

Formulation-related improvement and the bioavailability distinction

The formulation studies demonstrated that carrier design can improve curcumin dissolution, chemical stability, controlled release, cellular delivery, or biological potency.[1–3,13,14,17] Nano-sized formulations may enhance apparent solubility and intracellular delivery, whereas ionic-liquid-mediated systems can markedly improve aqueous dispersion and chemical stability.[2,3,17] However, bioavailability is a pharmacokinetic concept that requires direct measurement of systemic exposure or tissue availability.

Most included formulation studies did not report plasma curcumin concentrations, area under the concentration–time curve, maximum plasma concentration, time to maximum concentration, pharmacokinetic half-life, or tissue distribution.[1–3,13,14,17] Therefore, improved solubility, dissolution, cellular uptake, or in vitro potency should not be interpreted as definitive evidence of enhanced systemic bioavailability.

Future comparative studies should use matched curcumin-equivalent doses, standardized carrier characterization, free-curcumin and blank-carrier controls, pharmacokinetic and biodistribution analyses, and direct measurement of curcumin concentrations in tumor tissues. Without these comparisons, stronger in vitro activity may reflect increased local exposure rather than an inherently superior therapeutic mechanism.

Translational implications

The convergence of signaling pathways identified in this review suggests that curcumin may be investigated as a multi-target adjunct capable of modulating proliferative signaling, epithelial–mesenchymal transition, matrix remodeling, stemness, and treatment resistance.[4,5,9,11–13,23–26] This

pleiotropic activity may be particularly relevant in heterogeneous tumors in which multiple pathways contribute simultaneously to progression and metastatic dissemination.

Among the formulation strategies reviewed, the ionic-liquid-mediated system showed the most substantial improvement in aqueous solubility (~8,750-fold increase) with selective cancer-cell toxicity[3] while spanlastics demonstrated the strongest anticancer activity among the particulate systems tested. [1] These two approaches may therefore warrant priority in future pharmacokinetic and in vivo validation studies, ahead of formulation types with comparatively modest or unconfirmed biological advantages.

The most informative future studies should combine optimized formulations with clinically relevant orthotopic or spontaneous metastasis models, standard-of-care treatments, pharmacodynamic biomarkers, and long-term safety assessment. Clinical trials should also distinguish among dietary turmeric, conventional curcumin supplements, and advanced curcumin formulations because these interventions are not equivalent in composition, dosage, absorption, metabolism, or systemic exposure. Until such evidence becomes available, curcumin should be regarded as a promising preclinical nutraceutical candidate rather than a clinically established anticancer intervention.

Strengths and limitations

A strength of this review is its integrated synthesis of biological effects and formulation science across 15 preclinical studies. Separating native-curcumin studies from formulation studies reduced conceptual confusion and allowed physicochemical outcomes to be interpreted alongside cancer-related outcomes.

The review also has important limitations. Most evidence was generated in two-dimensional cell cultures, and only a minority of studies assessed tumor growth or metastasis in animals. Cancer types, formulations, dose units, exposure times, assays, and outcome definitions were highly heterogeneous, preventing meta-analysis. Several studies used complex stimulation or treatment contexts, and formulation studies did not consistently include matched free-curcumin and blank-carrier controls, while direct pharmacokinetic bioavailability was rarely measured. The review was also deliberately scoped to preclinical evidence, so recent clinical and translational studies fell outside the eligibility criteria and were not systematically searched. Finally, publication bias could not be formally assessed, as few included studies reported negative or null findings—a pattern consistent with a broader tendency in the preclinical curcumin literature to selectively report positive outcomes. These scope- and reporting-related constraints should be kept in mind when interpreting the translational relevance and overall direction of the synthesized evidence.

CONCLUSION

Preclinical evidence indicates that curcumin exerts broad antiproliferative and anti-metastatic effects across multiple in vitro and, to a lesser extent, in vivo cancer models. These effects involve suppression of cell-cycle and survival signaling, induction of apoptosis, reduced migration and invasion, reversal of EMT, inhibition of matrix metalloproteinases, and attenuation of stemness. Among the identified pathways, TGF-β/Smad2/3 and PI3K/Akt/mTOR-related signaling were supported by the most consistent and mechanistically detailed evidence, including in vivo confirmation, whereas Hedgehog/Gli1, Wnt/β-catenin/Bclaf1, NF-κB/PRL-3, miR-301a-3p/STAT3, and TRIM2/mTOR were each supported by single-study evidence and warrant cautious interpretation pending replication. This body of evidence should be regarded as demonstrating curcumin's bioactivity rather than its clinical efficacy: heterogeneity in cancer models, formulations, doses, and outcome measures, together with the predominance of in vitro over in vivo data, limits the extent to which these findings can be generalized to clinical settings. Among the formulation strategies reviewed, ionic-liquid-mediated solubilization and spanlastic systems showed the most substantial gains in solubility and anticancer potency, respectively, and may warrant priority in future pharmacokinetic and in vivo validation. However, these improvements do not yet establish systemic bioavailability or clinical effectiveness. Curcumin should therefore be regarded as a promising food-derived nutraceutical candidate—supported at present by bioactivity evidence rather than clinical efficacy evidence—requiring standardized formulations, rigorous pharmacokinetic and safety evaluation, clinically relevant metastasis models, and well-designed human trials before consideration as an adjunctive intervention in cancer care.

Ethical Considerations

As this scoping review involved the synthesis of publicly available published literature and did not include human participants or primary data collection, institutional ethics approval and informed consent were not required.

BIBLIOGRAPHY

1. Almutairi JA et al. An assessment of curcumin, curcumin spanlastics nanoparticles, and curcumin nanocrystals as possible drug delivery systems with antimicrobial, antioxidant, and antitumor activities. BMC Biotechnology. 2026;26(1):55. https://doi.org/10.1186/s12896-026-01153-x

2. Bahreyni Toossi MT et al. Dual role of Curcumin and nano-formulations in radiotherapy: sensitizing cancer cells and protecting normal cells. Molecular Biology Reports. 2026;53(1):190. https://doi.org/10.1007/s11033-025-11360-y

3. Bisht M et al. Superbase ionic liquid mediated solubilization of curcumin for improved bioavailability and anticancer efficacy. Scientific Reports. 2026;16(1):17923. https://doi.org/10.1038/s41598-026-44082-7

4. Cao L et al. Curcumin inhibits hypoxia-induced epithelial-mesenchymal transition in pancreatic cancer cells via suppression of the hedgehog signaling pathway. Oncology Reports. 2016;35(6):3728–3734. https://doi.org/10.3892/or.2016.4709

5. Chen X, Tian F, Lun P, Feng Y. Curcumin Inhibits HGF-Induced EMT by Regulating c-MET-Dependent PI3K/Akt/mTOR Signaling Pathways in Meningioma Lin H, editor. Evidence-Based Complementary and Alternative Medicine. 2021;2021:1–10. https://doi.org/10.1155/2021/5574555

6. Hanahan D. Hallmarks of Cancer: New Dimensions. Cancer Discovery. 2022;12(1):31–46. https://doi.org/10.1158/2159-8290.CD-21-1059

7. Hewlings S, Kalman D. Curcumin: A Review of Its Effects on Human Health. Foods. 2017;6(10):92. https://doi.org/10.3390/foods6100092

8. Hooijmans CR et al. SYRCLE's risk of bias tool for animal studies. BMC Medical Research Methodology. 2014;14(1):43. https://doi.org/10.1186/1471-2288-14-43

9. Hu C et al. Anti-metastasis activity of curcumin against breast cancer via the inhibition of stem cell-like properties and EMT. Phytomedicine. 2019;58:152740. https://doi.org/10.1016/j.phymed.2018.11.001

10. Lambert AW, Pattabiraman DR, Weinberg RA. Emerging Biological Principles of Metastasis. Cell. 2017;168(4):670–691. https://doi.org/10.1016/j.cell.2016.11.037

11. Li M et al. Curcumin inhibits the invasion and metastasis of triple negative breast cancer via Hedgehog/Gli1 signaling pathway. Journal of Ethnopharmacology. 2022;283:114689. https://doi.org/10.1016/j.jep.2021.114689

12. Liang Y et al. Curcumin inhibits the viability, migration and invasion of papillary thyroid cancer cells by regulating the miR-301a-3p/STAT3 axis. Experimental and Therapeutic Medicine. 2021;22(2):875. https://doi.org/10.3892/etm.2021.10307

13. Liu S, Zhou S, Wang B, Jia Z. Effects of curcumin nanoparticles on the proliferation and migration of human ovarian cancer cells assessed through the NF-κB/PRL-3 signaling pathway. International Immunopharmacology. 2024;141:112964. https://doi.org/10.1016/j.intimp.2024.112964

14. Moawad M et al. Comparative multi-pathway inhibition of breast cancer by micro-and nano-formulated Curcumin. Molecular Biology Reports. 2026;53(1):411. https://doi.org/10.1007/s11033-026-11506-6

15. Naksuriya O, Okonogi S, Schiffelers RM, Hennink WE. Curcumin nanoformulations: A review of pharmaceutical properties and preclinical studies and clinical data related to cancer treatment. Biomaterials. 2014;35(10):3365–3383. https://doi.org/10.1016/j.biomaterials.2013.12.090

16. Nieto MA, Huang RY-J, Jackson RA, Thiery JP. EMT: 2016. Cell. 2016;166(1):21–45. https://doi.org/10.1016/j.cell.2016.06.028

17. Özerkan D, Danışman-Kalındemirtaş F, Kariper İA. Synthesis and characterization of NIR-sensitive curcumin-gelatin nanoparticles for targeted drug delivery in 3D colon cancer. Scientific Reports. 2026;16(1):12167. https://doi.org/10.1038/s41598-026-42199-3

18. Page MJ et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29:n71. https://doi.org/10.1136/bmj.n71

19. Rethlefsen ML et al. PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Systematic Reviews. 2021;10(1):39. https://doi.org/10.1186/s13643-020-01542-z

20. Schneider K et al. “ToxRTool”, a new tool to assess the reliability of toxicological data. Toxicology Letters. 2009;189(2):138–144. https://doi.org/10.1016/j.toxlet.2009.05.013

21. Sharifi-Rad J et al. Turmeric and Its Major Compound Curcumin on Health: Bioactive Effects and Safety Profiles for Food, Pharmaceutical, Biotechnological and Medicinal Applications. Frontiers in Pharmacology. 2020;11. https://doi.org/10.3389/fphar.2020.01021

22. Tomeh MA, Hadianamrei R, Zhao X. A Review of Curcumin and Its Derivatives as Anticancer Agents. International Journal of Molecular Sciences. 2019;20(5):1033. https://doi.org/10.3390/ijms20051033

23. Yin J et al. Curcumin reverses oxaliplatin resistance in human colorectal cancer via regulation of TGF-β/Smad2/3 signaling pathway. OncoTargets and Therapy. 2019;Volume 12:3893–3903. https://doi.org/10.2147/OTT.S199601

24. Yu H et al. Curcumin suppresses colorectal cancer by inhibiting TRIM2 and mTOR signaling. Translational Oncology. 2025;61:102517. https://doi.org/10.1016/j.tranon.2025.102517

25. Zhang L et al. Curcumin inhibits metastasis in human papillary thyroid carcinoma BCPAP cells via down-regulation of the TGF-β/Smad2/3 signaling pathway. Experimental Cell Research. 2016;341(2):157–165. https://doi.org/10.1016/j.yexcr.2016.01.006

26. Zhao Z et al. Curcumin inhibits invasion and metastasis of human hepatoma cells through Bclaf1-mediated Wnt/β-catenin signalling. Food and Agricultural Immunology. 2022;33(1):664–676. https://doi.org/10.1080/09540105.2022.2113864