Review Article

# Clinical Antitumor effects of Curcumin in Prostate Cancer Environment: A Meta-Analysis

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## Abstract

**Background:** Curcuma longa L. is increasingly acknowledged as a chemopreventive agent for cancer and is currently being administered to humans. Nonetheless, the limited number of clinical trials conducted for prostate cancer treatment is significant. Our objective was to conduct a meta-analysis study to evaluate curcumin's tumor-inhibitory effects in humans.

**Materials and Methods:** PubMed, Embase, Scopus, and Web of Science databases were searched until October 2024 to retrieve relevant articles. The RAYYAN intelligence tool for systematic reviews was incorporated for screening studies. STATA v18 software was used to conduct the meta-analysis. Egger's test for publication bias assessment was implemented. The JBI critical appraisal tool was used to evaluate the qualities of the included studies. A plot digitizer was used to extract digital data.

**Results:** This meta-analysis evaluated the effects of curcumin on prostate cancer. Eight studies involving 638 participants were included out of 1,523 articles. The analysis showed that curcumin significantly reduces prostate cancer incidence, with a pooled effect size of -0.91 (95% CI: [-1.68, -0.14], P = 0.02). The results indicated significant heterogeneity among studies, though a slight publication bias was noted.

**Conclusion:** Curcumin demonstrated a favorable effect on prostate cancer treatment and exhibited inhibitory properties toward prostate tumor growth, thereby providing substantiation for additional clinical investigations. Including a limited number of studies resulted in a significant degree of heterogeneity among the included studies, which is a critical point to recognize. As a result, additional randomized controlled trials are necessary to thoroughly evaluate curcumin's efficacy in humans.

**Keywords:** Prostate cancer, Anti-tumor, Curcumin, Turmeric

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## Introduction

Prostate cancer (PCa) is a malignant tumor linked to elevated morbidity and mortality rates. Statistical data reveal that in 2020, there were an estimated 1,414,259 newly diagnosed instances of prostate cancer globally, accounting for around 7.3% of all newly diagnosed cancer patients and establishing it as the second most prevalent cancer type. Furthermore, prostate cancer is projected to result in 375,304 fatalities, representing approximately 3.8% of all cancer-related deaths[1]. The incidence and mortality rates of prostate cancer have

**Table 1.** Search strategies and results of the search procedure.

| Database | Search strategy | Results |
|---|---|---|
| **PubMed and Embase** | ((((curcumin[Title/Abstract]) OR ("Curcumin"[Mesh])) OR (Turmeric[Title/Abstract]))) AND ((("prostate cancer"[Title/Abstract]) OR ("Prostatic Neoplasms"[Mesh])) OR (prostate[Title/Abstract])) | 515 |
| **WOS** | (TS=("prostate cancer") OR TS=("Prostatic Neoplasms")) OR TS=("prostate tumor") AND (TS=(curcumin)) OR TS=(Turmeric) | 992 |
| **Scopus** | (TITLE-ABS-KEY("Curcumin") OR TITLE-ABS-KEY(turmeric)) AND (TITLE-ABS-KEY("prostate cancer") OR TITLE-ABS-KEY(prostate)) | 1732 |

significantly risen within the context of an increasingly aged population. Forecasts suggest that by 2040, the worldwide occurrence of prostate cancer is expected to rise to almost 2.3 million new cases, with 740,000 deaths[1].

Prostate cancer has become a crucial factor influencing health and mortality in men. The primary therapeutic approaches for prostate cancer consist of surgery, radiation, and chemotherapy. Nonetheless, these interventions possess limitations and may negatively impact patients' quality of life; therefore, it is essential to tackle the shortcomings of current therapies by developing and deploying innovative anticancer drugs that demonstrate improved therapeutic efficacy and reduce adverse effects. In this context, herbal extracts have received significant attention, supported by scientific studies demonstrating their capacity to impede tumor growth[2, 3].

Curcumin, a polyphenol extracted from turmeric, is frequently utilized in cooking due to its antioxidant, antibacterial, and anti-inflammatory characteristics[4]. A previous meta-analysis has demonstrated curcumin's therapeutic potential for treating malignant tumors[5].

Currently, there is an absence of published meta-analyses evaluating the efficacy of curcumin in prostate cancer treatment. Curcumin has shown a notable impact on several prostate cancer cell types when employed as a therapeutic intervention[6]. Therefore, we aimed to examine curcumin's therapeutic effects and potential importance in human models of prostate cancer to provide a basis for clinical research and pharmaceutical development.

# Methods

The current study is a systematic review and meta-analysis that adheres to the principles outlined in the PRISMA. Checklist[7]. The study protocol has been registered within the Open Science Framework (OSF). (DOI 10.17605/OSF.IO/EW93X)

**Search strategy:** A comprehensive and systematic search was conducted to identify clinical studies evaluating the antitumor effects of curcumin in the context of prostate cancer. The search strategy was developed according to the PRISMA 2020 guidelines and tailored to each electronic database. We searched PubMed, Scopus, and Web of Science from inception to October 2024. Using Boolean operators, the search terms combined Medical Subject Headings (MeSH) and free-text keywords related to curcumin and prostate cancer.

The core search string included: (“curcumin” OR “diferuloylmethane”) AND (“prostate cancer” OR “prostatic neoplasms” OR “prostate tumor”) AND (“clinical trial” OR “randomized controlled trial” OR “human study” OR “patients”).

Additional filters were applied to include only studies involving human participants and those published in English. Reference lists of included studies and relevant reviews were manually screened to identify any additional eligible articles not captured through the database search. All records were imported into EndNote for deduplication, and two independent reviewers screened the titles, abstracts, and full texts for eligibility based on predefined inclusion and exclusion criteria (Table 1).

**The inclusion and exclusion criteria:** We included studies that met the following criteria: (1) involved human participants diagnosed with prostate cancer; (2)

investigated the clinical effects of curcumin or curcumin-based formulations on tumor-related outcomes (e.g., tumor size, PSA levels, progression-free survival); (3) were designed as randomized controlled trials (RCTs), non-randomized clinical trials, or prospective cohort studies with comparator groups; and (4) reported sufficient quantitative data to enable effect size estimation. Preclinical studies, reviews, conference abstracts, commentaries, case reports, and editorials were excluded. Any discrepancies between reviewers during the screening or data extraction process were resolved through discussion and consensus; if disagreement persisted, a third independent reviewer was consulted to reach a final decision.

**Data extraction:** Data for this study were extracted by two individuals separately, and the results were compared by a third reference examiner (F.Z, S) to recognize and resolve any discrepancies before entering the analysis process (Table 1). Author A.S. extracted the author, year, country, number of samples, enzyme activities, and brain extraction site for quantitative study analysis.

**Quality assessment of studies:** The JBI critical appraisal checklist was used to evaluate the quality assessment of selected studies; this criterion assesses study selection domains, group comparability, and study results[8].

**Statistical analysis:** Data analysis was conducted using STATA Version 18 software. The results were displayed as a standard mean difference with a 95% confidence interval, illustrated graphically in a forest plot. The variability among the qualifying studies was evaluated using the identical program. The random effects model was utilized in instances with substantial heterogeneity (I2>50%). A sensitivity analysis was conducted by omitting outlier studies and re-executing the meta-analysis. This enabled us to guarantee the dependability and consistency of our results. We utilized Egger's and Begg's plots to assess the potential for publication bias.

# Results

**Study Selection and Characteristics:** PubMed, Scopus, Embase, and Web of Science database searches identified one thousand five hundred twenty-three records. After removing 364 duplicates, 1,159 articles were screened by title and abstract. Of these, 1,150 were excluded for not meeting the inclusion criteria. Nine full-text articles were assessed for eligibility, and one was excluded due to inappropriate study design and inaccessible data, resulting in the inclusion of eight studies comprising 638 participants (351 in treatment groups and 287 in control groups) (Figure 1).

The included studies were conducted in diverse geographical regions, including China, Iran, Japan, Australia, England, Korea, and France. Participants' mean age ranged from approximately 67 to 70 years. Across the studies, curcumin was administered in various formulations, including nano-micellar, oral capsules, and polyphenol-rich combinations, at doses ranging from 1.44 g/day to 8 g/day, with treatment durations spanning from several weeks to six months. Comparator groups included placebos or standard care, and the reported clinical endpoints included PSA levels, symptom scores (e.g., IPSS), oxidative stress biomarkers, and progression-free survival (PFS) rates.

**Meta-Analysis Findings:** Using a random-effects model, the pooled analysis showed that curcumin significantly reduced prostate cancer burden, with a pooled standardized mean difference (SMD) of -0.91 (95% CI: [-1.68, -0.14], p= 0.02), favoring the curcumin treatment group over controls (Figure 2). This finding supports the antitumor efficacy of curcumin as a complementary therapeutic agent.

While initial heterogeneity appeared substantial based on $I^2$ statistics, further exploration using the Galbraith plot (Figure 3) suggested that heterogeneity could be partially attributed to differences in study design and population characteristics rather than statistical inconsistency alone. Sensitivity analyses—conducted by iteratively removing individual studies—did not significantly alter the overall effect size, confirming the robustness of the primary findings.

**Risk of Bias and Publication Bias:** All included studies underwent quality assessment using the JBI checklist, with most studies rated as moderate to high quality. However, a few lacked detailed reporting on blinding and outcome assessor masking. Funnel plot analysis (Figure 4) and Egger's test revealed a slight asymmetry, indicating minor publication bias, potentially due to the preferential publication of studies

with positive outcomes.

the small number of studies, exploratory comparisons

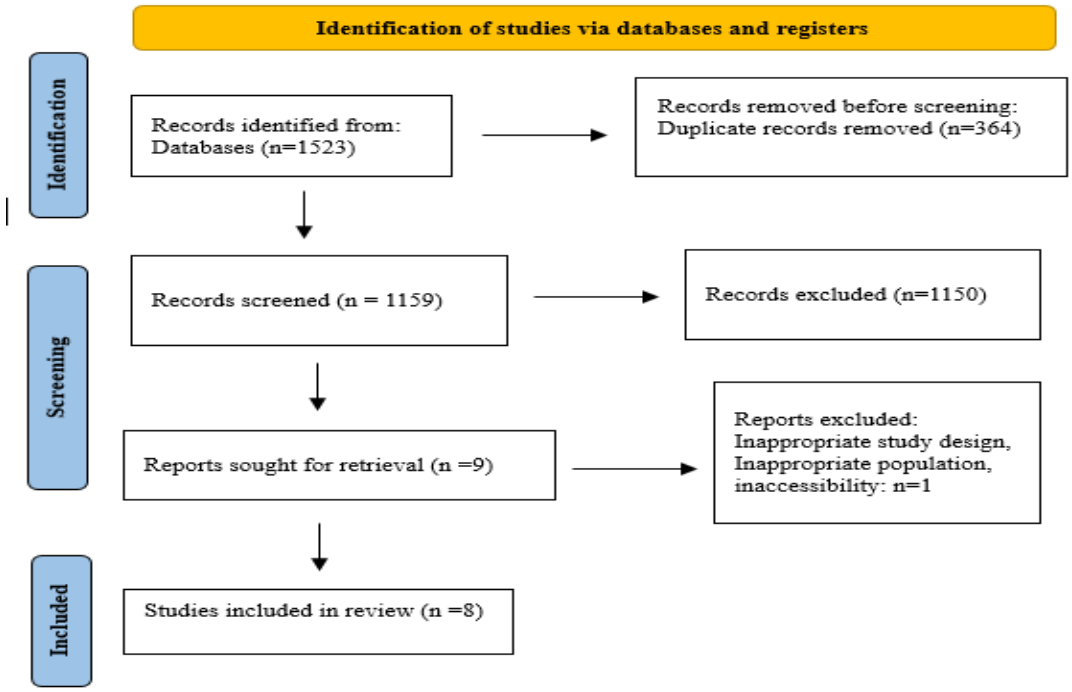


**Figure 1.** PRISMA flowchart of the study selection procedure.

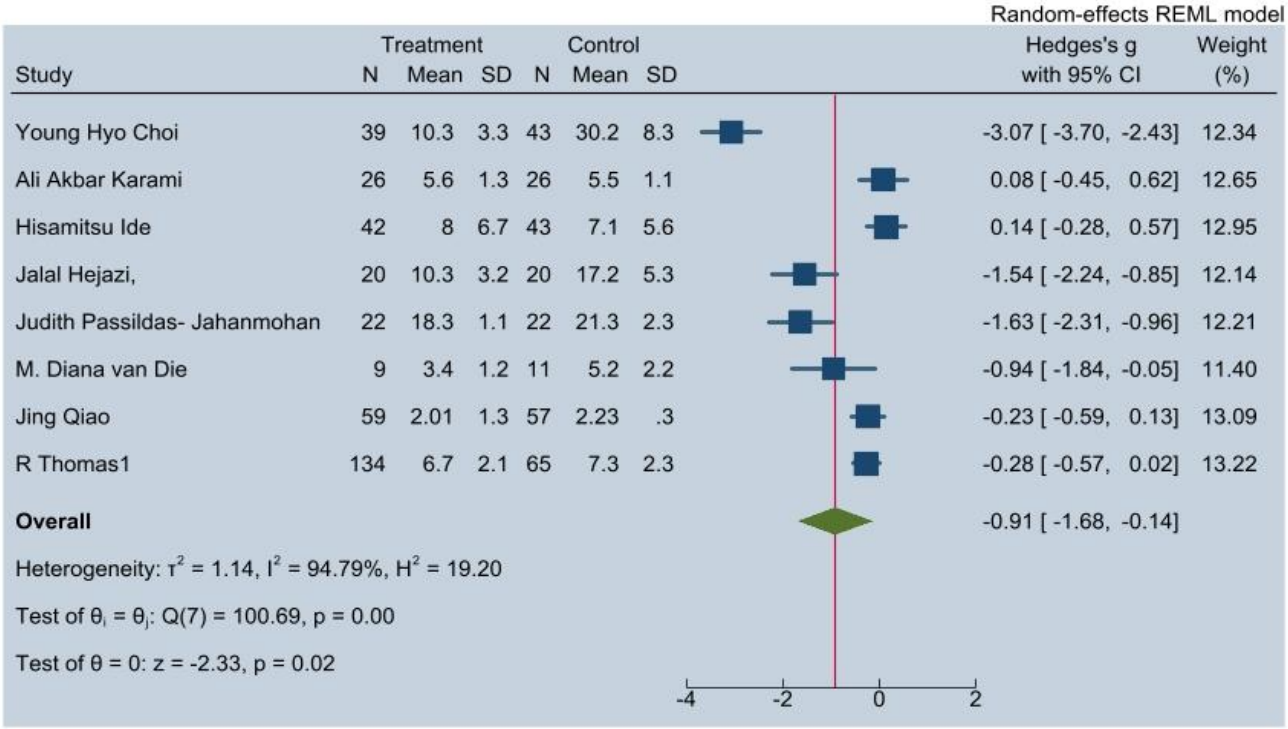


**Figure 2.** Forest plot of PSA standard mean difference levels in groups before and after receiving curcumin.

**Subgroup and Sensitivity Analyses:** Although formal subgroup meta-analyses were limited due to the small number of studies, exploratory comparisons suggest that nano-formulated curcumin and combination therapies (e.g., curcumin with isoflavones or

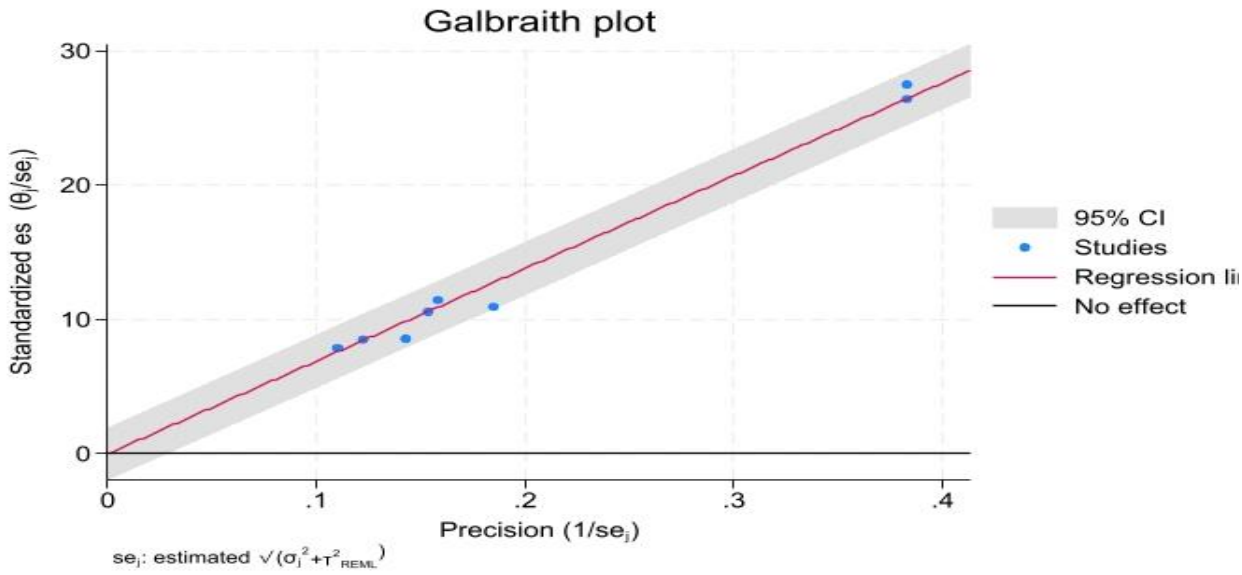


**Figure 3.** Galbraith plot of the $I^2$ test demonstration of heterogeneity amongst studies.

docetaxel) may yield stronger biochemical improvements (e.g., PSA suppression and IPSS score reduction) than standard formulations. However, effects were inconsistent across studies due to variability in trial duration, bioavailability, and baseline patient characteristics.

## Discussion

Patients with prostate cancer treated with curcumin participated in a randomized, placebo-controlled study conducted by CHOI and colleagues. The funding shows oral curcumin therapy was safe and well tolerated (1440 mg/day for 6 months). Curcumin's nontoxicity, safety, and tolerability at doses up to 8 g/day are well-proven based on multiple human trials. This study found no difference in the total off-treatment duration between the two groups, even though PSA advancement was noticeably slower in the curcumin group during the first six months. Additionally, curcumin is an active iron chelator that causes iron-deficient anemia in mice for those with low iron levels, which renders it ineffective. There was no delay in administration or discontinuation in this study because of the study's medication[9]. This meta-analysis indicates that curcumin has a significant tumor-inhibitory effect on prostate cancer. The findings suggest that curcumin may effectively reduce the incidence of prostate cancer among patients. This reduction was consistent across the included studies, which involved a diverse participant pool from various countries, enhancing the generalizability of the results.

Akbari Karami et al. conducted a double-anonymized randomized trial to evaluate the effectiveness of nano-micellar curcumin on the biomedical indicators of BPH. Following three months of consumption of nano-micellar curcumin, their study, which appears to be unique, showed that IPSS had minor to intermediate effectiveness. There were certain restrictions on this investigation. Despite being statistically significant (p-value: 0.01), the changes in IPSS (- 1.97 (0.73)) did not approach the substantial effect size and, more importantly, the MCID (MCID: 3). This result suggests that the study was unable to establish clinical significance and bolsters the need for additional research with larger sample sizes, higher dosages, and longer intervention durations[10].

This study aimed to assess the possible effectiveness of curcumin, isoflavones, and their combination as preventative measures against prostate cancer. The study's primary conclusions are that curcumin and isoflavone therapy improve the suppression of PSA generation. In this study, PSA levels dramatically decreased in the supplement-treated subgroup compared with the placebo group. A disadvantage of this initial clinical research was that the patients in the cohort were not controlled for the content of their meals

and most likely had previously been on diets high in curcumin or soy isoflavones[11].

The present investigation revealed that curcumin can increase TAC and decrease SOD activity in the plasma of patients with prostate cancer after radiation. Curcumin at the recommended dosage did not exhibit any radiosensitizing or prooxidant characteristics in this investigation; nevertheless, the decrease in SOD and catalase activity might be interpreted in the same way that Javvadi et al. did for TxnRd1. The authors concluded that curcumin increases oxidative stress within cancer cells and inhibits the antioxidant enzymes that counteract this action, making it radiosensitizing[12].

This study was mCRPC's first randomized, double-anonymized investigation. The study aimed to determine whether curcumin and docetaxel improved patient outcomes, specifically PFS. However, the findings of the interim analysis did not support the need to conduct more research. There are a few limitations to this study, such as the small sample size due to the early discontinuation of the interim analyses and the fact that the curcumin titration could have been done for all 50 patients rather than just a select few to support the findings on curcumin bioavailability. According to the study's findings, oral curcumin plus docetaxel at the regimen under investigation (6 g/d for 7 days) does not increase progression-free survival or overall survival in patients with mCRPC[13].

This study aimed to evaluate the feasibility of a randomized study on the phytotherapeutic combination of broccoli sprouts, green tea, resveratrol, and turmeric in males with BCR in a limited number of participants. The poor recruitment rate and resulting lower participant numbers were the primary limitations of this study. PSA kinetics and other outcome markers were not sufficiently powered to detect effects in this study. However, in this small sample, randomization did not evenly assign patients treated with radiation and surgery to active and placebo groups[14].

Qiao et al. investigate to support the hypothesis that IPSS-S is mainly affected by prostatitis and that curcumin has a significant anti-inflammatory effect on prostatitis. While both groups in this study saw substantial improvements in PV, Qmax, IPSS total, IPSS-V, IPSS-S, and QoL ratings from baseline following therapy, the IPSS-S and QoL scores demonstrated a superior and noticeably more significant improvement. This is the first study to assess how curcumin and BSM therapy affect BMI, body weight, and PPF in patients with BPH. The BSM group in this study did not show statistically significant differences in BMI, WC, or PPFT compared to the baseline. In contrast, the curcumin + BSM group showed substantial differences in WC and PPFT without a significant difference in BMI. There are various restrictions on the current investigation. Initially, this prospective study was planned as a single-center trial with limited clinical data and a comparatively small number of patients enrolled. Second, a 6-month follow-up time is relatively brief when researching a chronic illness[15].

With 50–70% of men with prostate cancer reportedly taking "over-the-counter" supplements, this statistically valid double-blind randomized controlled trial has shown a significant short-term benefit on PSA. The study's first weakness was the relatively short intervention period of six months. While this is sufficient to identify an early difference, a more extended design would rule out the idea that the effect was transient, given that men are frequently monitored for many years. The second limitation of this study was that it relied on PSA measurement with other formal indicators of disease progression, such as MRI and biopsy. This inclusion would have decreased the recruitment rate and added complexity, even while biopsy would have improved scientific competency because not all men now consent to a repeat intervention. Additionally, given the sponsorship level available, the expense of MRI before and after the trial period would have been prohibitive[16].

**Limitations:** This meta-analysis has several limitations that should be acknowledged. First, the number of included studies was relatively small (n=8), which limits the statistical power and generalizability of the findings. Second, significant heterogeneity was observed across studies regarding curcumin formulations, dosages, treatment durations, and outcome measures, which could have influenced the pooled effect size and contributed to variability in results. Third, the included studies varied in design quality, and although the JBI critical appraisal checklist was used, not all studies fully met the highest

methodological standards. Fourth, some studies included in the analysis lacked detailed reporting on dietary control, prior supplement use, or concurrent therapies, which may have acted as confounders. Fifth, the follow-up durations in several trials were short, limiting the ability to assess the long-term effects of curcumin on disease progression or survival outcomes. Finally, a slight publication bias was detected, suggesting that studies with negative or null results may be underrepresented in the literature.

## Conclusion

This meta-analysis provides preliminary clinical evidence supporting the tumor-inhibitory effects of curcumin in the management of prostate cancer. Curcumin was associated with a statistically significant reduction in prostate cancer burden, reinforcing its potential role as a complementary therapeutic agent. Despite promising findings, the limited number of high-quality clinical trials, intervention variability, and methodological constraints underscore the need for more rigorous, large-scale, randomized controlled trials. Future studies should aim to standardize curcumin formulations, control for dietary and pharmacological confounders, and evaluate long-term clinical outcomes better to define its therapeutic role in prostate cancer care.

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None.

## Conflict of interest

The authors further declare that they have no conflict of interest.

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None.

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