Table 1: Systematic reviews of curcumin for oral mucositis

Source: CAM-Cancer Collaboration. Curcumin for oral mucositis [online document]. Curcumin | Oral mucositis, October 2026.

Review characteristics	PICO of included studies	Results and conclusions	Assessment
Berkovitz, S., Collaço, N., Dolakova, K., & Hughes, J. (2026). *A systematic review of turmeric/curcumin for prevention and treatment of oral mucositis due to radiotherapy and/or chemotherapy for head and neck cancer. Journal of Integrative and Complementary Medicine*. Advance online publication. https://doi.org/10.1177/27683605261426992			
Type of review and data synthesis Systematic review with narrative synthesis. **Studies: n and design** 9 RCTs **Search strategy:** **Databases** MEDLINE and CINAHL **Dates** From database inception to 20 October 2025 **Risk of bias assessment** Cochrane Risk of Bias tool RoB 2.0	**Studies and participants** 503 participants Adults diagnosed with head and neck cancer, receiving radiotherapy with or without chemotherapy, and at risk of or experiencing treatment-induced oral mucositis. **Interventions** Turmeric/curcumin administered as oral capsules, nanomicelle curcumin capsules, mouthwash, oral rinse, gel, or powder suspension. **Control** Placebo, benzydamine mouthwash, chlorhexidine mouthwash/gel, povidone-iodine mouthwash, or standard care. **Outcome measures** Oral mucositis severity: World Health Organization (WHO) Oral Mucositis Scale, Radiation Therapy Oncology Group (RTOG) scale, Oral Mucositis Assessment Scale (OMAS), National Cancer Institute Common Toxicity Criteria (NCI-CTC), Common Terminology Criteria for Adverse Events (CTCAE). Pain: Numerical Rating Scale (NRS) Burning sensation: Visual Analogue Scale (VAS) Patient-reported symptoms: Patient Reported Oral Mucositis Symptoms (PROMS) Ulceration/Erythema: Area measurement using transparent checkered paper	**Results for risk of bias assessment of primary studies included in the review** Overall, 5 of the 9 included RCTs were judged to have a low risk of bias, while 2 studies had some concerns and 2 studies were rated as high risk of bias. Two of the studies were assessed as high risk of bias from bias in measurement of the outcome, and selection of the reported results. Two studies were also evaluated as having some concerns for bias arising from the randomization process. **GRADE** The GRADE assessment rated the certainty of evidence as low for both oral mucositis severity and weight loss. The evidence was downgraded primarily because of imprecision resulting from small study sample sizes and suspected publication bias. **Results for outcome measures** ***Oral mucositis severity:*** In eight of the nine studies included, there were significant improvements on WHO OM score, grade, and delayed onset. P-values ranged from <0.0001 to 0.005 ***Time to onset of mucositis:*** Four studies reported that patients receiving turmeric/curcumin generally developed mucositis later during radiotherapy (p >0.01). One study did not find a statistically significant delay in maximum OM grade ***Weight lost:*** Three studies reported significantly less weight loss in patients receiving turmeric/curcumin. . Reduced weight loss likely reflects better oral function,	**Quality assessment of the SR** Moderate-high according to AMSTAR2. The authors only searched a limited number of databases. **Comments** Although the SR itself is of moderate quality, some limitations of the included RCTs were small and exploratory studies, heterogeneous in intervention (doses, formulation and mode of administration), comparators, outcome measures, poor safety reporting, and potential publication bias resulted in low-certainty evidence. While the authors did not conduct a formal assessment of publication bias, publication bias was suspected and discussed in the GRADE assessment.

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	Measure of treatment effect Mainly p-values comparing intervention and control groups for incidence, severity, risk, scores, onset time, pain scales, and quality-of-life measures	less pain, and improved ability to maintain nutritional intake during radiotherapy (p<0.014 - p<0.006) ***Pain:*** Four studies found statistically significant reductions in oral pain (p<0.001 - p=0.027). Reduced pain severity appeared to parallel improvements in mucositis severity. **Adverse events** Five of the included studies did not report adverse events. The remaining studies reported very few adverse events, with only mild transient nausea and mild oral burning sensations documented. No study reported any serious adverse events, severe toxicity, or treatment discontinuation due to turmeric/curcumin. **Conclusion** *"… This systematic review identifies significant gaps in research on turmeric for its (oral mucositis) management. Current evidence is too low quality to draw definitive conclusions about its effectiveness and safety. High-quality, well-designed studies are needed to assess its clinical efficacy, effectiveness, safety, acceptability, and cost-effectiveness."*	

Gutsche, L. C., Drefer, J., & Hüber, J. (2025). *Curcumin as a complementary treatment in oncological therapy: A systematic review*. European Journal of Clinical Pharmacology, 81, 1-33. https://doi.org/10.1007/s00228-024-03764-9

Type of review Systematic review with narrative synthesis **Studies: n and design** 34 RCTs **Search strategy:** *Databases* MEDLINE (Ovid), Embase (Ovid), Cochrane CENTRAL, PsycINFO (EBSCO), CINAHL (EBSCO) **Dates** From 1995 to January 2024 **Risk of bias assessment** Cochrane Risk of Bias tool RoB 2.0	**Participants** 2,580 participants (2,449 analyzed). Adults diagnosed with any type and stage receiving cancer treatment **Interventions** Oral curcumin supplementation (20 + RCTs), Curcumin mouthwash /rinse (8 RCTs), topical curcumin oral gel (3 RCTs), topical curcumin gel (3 RCTs), Intravenous curcumin (1 RCT) **Control** UC, Chlorhexidine, benzydamine, povidone-iodine, HPR Plus™ cream, aloe vera, Riboflavin placebo + paclitaxel **Outcome measures:**	**Results for risk of bias assessment of primary studies included in the review** Overall, the risk of bias was rated as high for 22/34 studies; twelve studies were rated as moderate risk of bias, and no studies were rated as low or unclear risk of bias. Most studies had issues with blinding, randomization, and unreliable concealment methods. **GRADE:** No GRADE assessment was conducted. **Results for outcome measures:** *Oral mucositis:* Twelve of the 13 RCTs showed significantly lower mucositis severity with curcumin versus placebo, chlorhexidine, benzydamine, or povidone-iodine. p < 0.001 to p = 0.003 across studies.	**Quality assessment of the SR:** Moderate according to the AMSTAR 2 checklist. Methods only partially described as this SR was part of guideline development and the authors did not provide a protocol registration. **Comments** Although the SR is of moderate quality, there is substantial heterogeneity in design, populations and outcome measures and pool effect estimates could not be calculated. The included studies had small sample sizes, and moderate/high risk of bias in the included studies. The review did not assess certainty of evidence using GRADE.

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	Oral mucositis (13 RCTs): WHO Oral Mucositis Scale, WHO Oral Toxicity Scale, OMAS, NCI-CTCAE, NCI-CTC v2, RTOG criteria. *Pain (11 RCTs):* Numerical Rating Scale (NRS), Visual Analogue Scale (VAS), McGill Pain Questionnaire-Short Form (MPQ-SF). *Radiation dermatitis (4 RCTs)*: Radiation Dermatitis Severity Scale (RDS), RTOG Skin Toxicity Criteria, NIH CTCAE *Quality of life (9 RCTs)*: EORTC QLQ-C30, EORTC QLQ-PR25, UW-QOL, FACT-P, Skindex-29. *Functional status (5 RCTs):* ECOG Performance Status, Karnofsky Performance Status *Survival (4 RCTs):* Overall Survival (OS), Progression-Free Survival (PFS), Time to Tumor Progression (TTP) *Prostate cancer progression (3 RCTs):* PSA levels, PSA progression rates *Tumor response (7 RCTs):* RECIST criteria, WHO Response Criteria, Pathologic Complete Response (pCR) *Body composition (2 RCTs):* Bioelectrical Impedance Analysis (BIA), body fat mass, skeletal muscle mass, BMI *Adverse events (13 RCTs)*: CTCAE, NCI-CTCAE, laboratory toxicity measures **Measure of treatment effect** Mean differences, risk ratios, proportions, hazard ratios (HRs), between-group mean differences, incidence rates**,** mean score differences, odds ratios, response rates, risk estimates	*Pain associated with oral mucositis:* Six out 11 RCTs showed significant reduction in oral pain with curcumin compared with placebo or active controls $p < 0.001$ to $p = 0.02$. *Radiation dermatitis (skin toxicity):* One out of four RCTs showed lower radiation dermatitis severity with curcumin SD -0.8 (-1.4, -0.2) $p = 0.008$. *Pain associated with skin toxicity*: One out of four RCTs reported lower pain scores with nanocurcumin during radiotherapy $p = 0.002$-0.045. *Weight loss*: Three out of 5 RCTs reported less weight loss with nanocurcumin/turmeric rinse/The remaining 2 RCTs did not show significant associations. *Body composition:* Thambamroong et al. (2022): improved muscle mass compared with placebo. Muscle mass change in kg: A: 0.46 (-0.2, 1.12), B: -1.05 (-2.34, 0.24) $p = 0.03$. The remaining RCT did not show significant associations. *Overall survival (OS):* Howells et al. (2019): improved OS in colorectal cancer (ITT analysis).HR = 0.339 (0.141, 0.815) $p = 0.016$. Howells et al. (2019): improved OS (per-protocol analysis).HR = 0.271 (0.106, 0.697) $p = 0.004$. The remaining 3 RCTs did not show significant associations. *Progression-free survival (PFS):* No significant results. *PSA progression*: One out of four RCTs reported lower PSA progression rate in prostate cancer.10.3% vs 30.2% progression $p = 0.0259$. *Tumor response:* Saghatelyan et al. (2020): objective response rate higher with curcumin + paclitaxel.ORR 50.7% vs 33.3% $p = 0.0145$. Santosa et al. (2022): higher remission rate in multiple myeloma.OR 75% vs 33.3% $p = 0.01$. The remaining 5 RCTs did not show significant associations	

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		Quality of Life (QoL): Two RCTs showed greater QoL improvement with curcumin, the remaining 7 RCTs did not show significant associations **Subgroup analysis** Overall, subgroup analyses suggested that the benefits of curcumin were most consistently observed among patients undergoing chemotherapy and/or radiotherapy for head and neck cancers, particularly for reducing oral mucositis, oral pain, and treatment-related weight loss. Some studies also suggested differential effects according to cancer type, treatment modality, baseline disease characteristics, or curcumin dose, but these findings were often based on small sample sizes and should be interpreted cautiously **Adverse events** The authors stated that multiple of the included RCTs reported adverse events. Only one study reported significantly more vomiting in the intervention group. The rest of the adverse events reported were minor (i.e., gastrointestinal symptoms such as nausea, diarrhea, abdominal discomfort, and vomiting). **Conclusion** "*Although studies showed some beneficial effects of curcumin administration on cancer therapy-related side effects, especially oral symptoms and weight loss, there were clear methodological weaknesses decreasing the reliability of these results*."	

Limbrunner, J., Doerfer, J., Pietschmann, K., Buente, J., Scharpenberg, M., & Huebner, J. (2025). *The influence of antioxidant supplementation on adverse effects and tumor interaction during radiotherapy: A systematic review*. Clinical and Experimental Medicine, 25, 258. https://doi.org/10.1007/s10238-025-01804-x			
Type of review: Systematic review with narrative synthesis **Studies: n and design** 39 RCTs, thereof 17 of curcumin/turmeric. **Search strategy:** **Databases** MEDLINE (Ovid), EMBASE (Ovid), CINAHL (EBSCO), Cochrane CENTRAL, and PsycINFO (EBSCO)	**Participants** 3,184 participants Adults (≥16 years) with cancer receiving radiotherapy, cancer type, or stage **Interventions** Curcumin/Turmeric preparations: 17 RCTs; Vitamin-based interventions: 11 RCTs. Flavonoids 8 RCTs. Glutathione 3 RCTs. Multiple antioxidant combinations 2 RCTs.	**Results for risk of bias assessment of primary studies included in the review** Overall, the risk of bias was rated as high for 23/39; ten studies were rated as some concerns, and six were rated as low risk of bias. Reasons for higher risk ratings included lack of blinding, absence of intention-to-treat analyses, incomplete outcome data, small sample sizes, and selective reporting of outcomes. **GRADE**	**Quality assessment of the SR** Moderate quality according to AMSTAR 2 checklist. No assessment of publication bias was reported. **Comments** Considerable clinical heterogeneity. The included studies varied widely in cancer types, stages, radiotherapy regimens, antioxidant agents, dosages, routes of administration, and

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Dates Search conducted in 2024 the authors did not state the date range for the search. **Risk of bias assessment** Cochrane Risk of Bias tool RoB 2	**Control** UC, placebo control, active control (Chlorhexidine mouthwash, benzydamine mouthwash, povidone-iodine, anesthetic/antimicrobial solution) **Outcome measures (primary outcomes)** *Oral mucositis (14 RCTs: Curcumin/tumerrc 12 RCTs, Vitamin C/E 2 RCTs)*: WHO Oral Mucositis Scale, CTCAE, Oral Mucositis Assessment Scale (OMAS), Oral Health Assessment Tool (OHAT), Numerical Rating Scale (NRS), PROMS. *Dermatitis/Radiodermatitis (8 RCTs: Vitamins C/E (2), Curcumin (3), Flavonoids (2), Glutathione (1)):* RTOG criteria, CTCAE, Radiation Dermatitis Severity Score, Skin Toxicity Assessment Tool, thermography, cutometer, mexameter. *Esophagitis (2 RCTs EGCG (green tea flavonoid)):* RTOG score, CTCAE, NRS, adjusted pain/dysphagia indices. *Xerostomia (1 RCT:Vitamin C + Vitamin E):* Xerostomia questionnaire, observer-rated xerostomia score, salivary scintigraphy, Xerostomia Short Form Inventory. Proctitis/Cystitis (1 RCT: curcumin): CTCAE (Common Terminology Criteria for Adverse Events **Measure of treatment effect** Odds Ratio, hazard Ratio Risk/percentage, mean differences, p-values, confidence interval.	No GRADE assessment was conducted. **Results for outcome measures** ***Oral mucositis*** *Curcumin* improved oral mucositis in eleven of twelve RCTs. Significant benefit reported; p-values ranged from <0.001 to 0.027. *Vitamin C* supplementation reduced mucositis severity in a dose-dependent manner. Significant benefit reported $p < 0.001$. *Vitamin E* mouth rinse reduced occurrence of oral mucositis. Significant benefit reported; $p = 0.038$. ***Esophagitis:*** EGCG reduced severity of radiation-induced esophagitis and associated pain. Significant benefit reported; A vs C $p < 0.001$; B vs C $p = 0.002$. ***Xerostomia:*** *Vitamin C + Vitamin E* improved xerostomia symptoms. Significant benefit reported; questionnaire $p = 0.007$; observer score $p = 0.008$; salivary scintigraphy $p = 0.01$ and $p = 0.009$. ***Radiation-induced dermatitis*** EGCG lowered incidence of grade ≥2 dermatitis. Significant benefit reported; $p = 0.008$. Curcumin reduced dermatitis severity (Ryan et al.). Mean difference = −0.8, 95% CI (−1.4, −0.2), $p = 0.008$. ***Proctitis/Cystitis:*** Curcumin showed no significant benefit. **Secondary outcomes** ***Tumor-Related outcomes*** Head and neck cancer recurrence: Higher plasma β-carotene associated with lower recurrence risk.HR = 0.54, (0.32, 0.91), $p < 0.05$. Second primary cancer (smokers receiving antioxidants during RT): Increased risk observed. HR = 2.41 (1.25, 4.64), $p = 0.03$. Death from first cancer (smokers receiving antioxidants during RT): Increased mortality observed.HR = 3.38, 95% CI (1.11, 10.34), $p = 0.04$.	outcomes measured. The included studies had small sample sizes.

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		Overall survival, disease-free survival, progression-free survival (several studies): No significant differences. ***<u>Quality of life</u>*** Acute radiation adverse effects (dietary β-carotene): reduced odds of toxicity. OR = 0.52, (0.28, 0.99). Acute radiation adverse effects (combined vitamin supplementation): reduced odds of toxicity. OR = 0.98, (0.52, 1.87) not significant. Urinary symptoms (curcumin, prostate cancer): reduced symptoms. Significant benefit reported; p = 0.011. Cardiac toxicity (LVEF decline): Vitamins C + E + NAC reduced decline in LVEF. Significant benefit reported; p = 0.008 (RTX only), p = 0.03 (CRTX); effect size not reported. ***<u>Weight Loss</u>*** Weight loss during radiotherapy: Curcumin reduced weight loss in multiple studies. Significant benefit reported; p-values from 0.003 to <0.001. **Adverse events** For the majority of the interventions, including curcumin, the studies assessed did not evaluate the adverse events. For one study evaluating EGCG, the authors reported a small number of participants experienced transient discomfort, skin prickling sensations, or pruritus after application. Most events were mild ***Conclusions*** "*In conclusion, we are not able to give a concrete recommendation for the use of antioxidants during radiotherapy. This is due to the very heterogeneous results of the studies, which predominantly had small numbers of included patients and generally a medium to high risk of bias.*"	

Abbreviations
CI: confidence interval
CRTX: Chemoradiotherapy
EGCG: epigallocatechin-3-gallate, a naturally occurring flavonoid
EORTC QLQ-C30– European Organization of Research and Treatment of Cancer Quality of Life Questionnaire
NRS: Numeric Rating Scale
RCT: randomized controlled trial
RoB: Cochrane Risk of Bias Tool version 1
RTX: Radiotherapy
SMD: standardized mean differences
SR: Systematic review

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UC: Usual care
VAS: Visual Analog Scale
WLC: Waitlist control
WMD: Weighted mean difference.
CTCAE, Common Terminology Criteria for Adverse Events
NCI-CTC, National Cancer Institute Common Toxicity Criteria
OM, oral mucositis
OMAS, Oral Mucositis Assessment Scale
T/C, turmeric/curcumin
RTOG, Radiation Therapy Oncology Group
WHO, World Health Organization.

***AMSTAR 2 Critical Domain Items**

1. Was the review protocol established a priori (e.g., registered in PROSPERO)?
2. Was the search comprehensive and included multiple databases, grey literature, and appropriate search strategies?
3. [Did the authors provide a list of excluded studies and justify the exclusions?]
4. Was the risk of bias (RoB) of included studies assessed using appropriate tools?
5. If a meta-analysis was conducted, were the methods used appropriate and clearly described?
6. Did the authors consider the RoB in individual studies when discussing the results?
7. Was publication bias assessed and discussed appropriately?

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