FNJN

İSTANBUL UNIVERSITY CERRAHPAŞA

Florence Nightingale Journal of Nursing

DOI: 10.5152/FNJN.2025.24153

Systematic Review

Effectiveness of Turmeric Contains on Chemo/Radiotherapy-Induced Oral Mucositis and Oral Dysfunction Among Head and Neck Cancer Patients: A Systematic Review of Randomized Controlled Trials

Priyanshi Dixit[1], Anjali Rathee[2], Uma Phalswal[3], Nipin Kalal[4]

[1]College of Nursing, Vardhman Mahavir Medical College & Safdarjung Hospital, New Delhi, India
[2]Department of Nursing Services All India Institute of Medical Sciences, New Delhi, India
[3]College of Nursing, AIIMS, Rishikesh, India
[4]College of Nursing, AIIMS, Jodhpur, India

Cite this article as: Dixit, P., Rathee, A., Phalswal, U., & Kalal, N. (2025). Effectiveness of turmeric contains on chemo/radiotherapy-induced oral mucositis and oral dysfunction among head and neck cancer patients: A systematic review of randomized controlled trials. *Florence Nightingale Journal of Nursing*, *33*, 0153, doi:10.5152/FNJN.2025.24153.

Abstract

AIM: The review elaborates on the efficacy of turmeric/curcumin formulations on chemo/radiotherapy-induced oral mucositis in patients with head and neck cancer.

METHODS: This systematic review was conducted; trials were included comparing turmeric/curcumin formulations with chlorhexidine/povidone-iodine/normal saline or any conventional practices in head and neck cancer patients. Studies published through May 2023 were identified using Medline, Web of Science, CINAHL, Embase, and the Cochrane Library. A systematic review was conducted, including a meta-analysis, following PRISMA guidelines. The methodology's quality was assessed using the Cochrane risk-of-bias tool.

RESULTS: Thirteen of the 14 studies found that turmeric formulation contributed to reducing the occurrence ($p < .0001$) and intensity of oral mucositis ($p = .001$) and significantly lesser incidence of secondary outcomes such as pain ($p = .001$), erythema ($p = .05$), dysphagia ($p < .05$), ulcer size ($p = .000$), burning sensation ($p < .001$), dermatitis ($p < .05$), and weight loss ($p < .001$) in the turmeric group. There was also a lesser incidence of treatment breaks (chemotherapy, radiotherapy, or chemoradiotherapy) due to the severity of mucositis and other complications. The risk of bias was judged as low for six studies (a score of five or higher), medium in three studies (four out of seven), and high risk for the other five.

CONCLUSION: The reviewers identified that turmeric formulations reduced the severity of oral mucositis. Future research is needed to determine the optimal dose and schedule of application of turmeric formulations in preventing oral mucositis. Healthcare providers can integrate turmeric formulations with standard oral care to alleviate mucositis.

Keywords: Chemo/radiotherapy-induced oral mucositis, head and neck cancer patients, turmeric contains

Introduction

Head and neck cancer (HNC) affects parts such as the oral cavity and its glands (salivary) nasal cavity, pharynx, and hypopharynx. Oral mucositis (OM) is a common and debilitating complication of chemotherapy (CT), radiotherapy (RT), or chemo-radiation in more than 95% of patients treated for HNC (Sonis, 2004). Mucositis produces pain or oral inflammation that may result in bleeding, trouble swallowing and eating, a lack of nutrition that results in weight loss, and prolonged hospitalizations (Anderson et al., 2018; Kanagalingam et al., 2017; Ribeiro da Silva et al., 2018) and can result in therapy (CT/RT/chemoradiotherapy (CRT)) discontinuation until symptoms subside. Oral mucositis is a functional disruption in the integrity of the oro-pharyngeal mucosa that causes discomfort in the mouth, restricted mouth opening, and a higher risk of

Received: July 18, 2024
Revision Requested: October 7, 2024
Last Revision Received: January 22, 2025
Accepted: March 17, 2025
Publication Date: July 24, 2025

Corresponding author: Nipin Kalal,
E-mail: kalalnipin@gmail.com

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License

infections such as oral candidiasis. Oral mucositis caused by CT often results in atrophy of the mouth's mucosal layer and ulcer formation in 100% of patients; OM caused by radiation therapy often affects up to 80% of patients (Lalla et al., 2014). After two weeks of starting radiation therapy, mouth soreness with erythema appears, and two weeks later, there is severe epithelial damage. Patients treated with concomitant RT and CT develop more severe OM, which might lead to a decrease in the dosage of CT or an interruption of RT; this could affect their survival rates as well as quality of life (Manzi et al., 2016; Scully et al., 2003; Trotti et al., 2003). Oral mucositis is divided into two categories based on severity: unbearable mucositis (grade 3 or higher) and tolerable mucositis (grades 1 and 2). A tolerable form of mucositis occurs in all patients receiving RT and is treatable, whereas intolerable mucositis requires an IV line for nutritional supplementation, a gastrostomy tube, and appropriate pain control. All of these issues may result in reduced radiation, reduced CT/RT dosages, or even radiation cessation (Bensinger et al., 2008).

Multinational Association of Supportive Care in Cancer/The International Society of Oral Oncology (MASCC/ISOO) has suggested a wide range of different therapies such as vitamins A, E, and L-glutamine ointment, local anesthetics, corticosteroids, and mouthwashes like chlorhexidine and povidone-iodine mouthwashes for mitigating OM in cancer patients, but none were proven to be used as standard treatment. There is currently a lack of scientific data addressing accepted practices for standard treatment, notwithstanding existing guidelines and recommendations for OM care. Therefore, finding a suitable replacement with few side effects is necessary. Herbal therapy offers a variety of pharmacological benefits with few side effects (Patil et al., 2015).

Turmeric (*Curcuma longa* L.) has various biological properties, including anti-inflammatory, antifungal, antibacterial, and anticancer properties, and helps in wound healing (Liczbiński et al., 2020; Nabavi et al., 2018). Research has demonstrated that curcumin, or turmeric, is beneficial in treating conditions like oral submucous fibrosis that may be cancerous (Rai et al., 2021). Curcumin inhibits tumor growth (Borges et al., 2017) and is useful in lessening the intensity of radiation dermatitis (Palatty et al., 2014; Ryan et al., 2013; Vaughn et al., 2016). Curcumin in the form of nano-micelles was employed by a study (Delavarian et al., 2019) and found suitable for preventing and lessening the intensity of OM. The same conclusion was also reported by Dharman et al. (Dharman et al., 2021) in their meta-analysis that to avoid delaying the development and intensity of OM, curcumin is a safe and well-tolerated medication. A systematic review (Normando et al., 2019) suggested the degree of mucositis, discomfort, erythema, and lesion size were all lowered by topical application of curcumin. When curcumin was given in both systemic and topical forms simultaneously, patients with submucous fibrosis demonstrated a considerable improvement in mouth opening and burning sensations, according to Rai et al. (Rai et al., 2021). In this review, all forms of curcumin were included to evaluate the benefits of all turmeric-containing formulations on chemo/radiotherapy-induced oral mucositis (C/RIOM) and oral dysfunction among HNC patients.

Curcumin is effective in reducing the severity of radiation dermatitis (Elad et al., 2013; Palatty et al., 2014; Ryan et al., 2013; Vaughn et al., 2016) and has strong antibacterial effects by inhibiting bacterial growth, epithelial cell adherence, and cellular invasion in mucositis (Lüer et al., 2014). Consequently, mucosal administration of curcumin via a topical route can be carried out, and this approach has been demonstrated to significantly enhance therapeutic efficacy. It is also potentially a promising strategy to treat mucositis, as it can regulate inflammation and bacterial load.

In a randomized controlled trial (RCT) the safety dose of curcumin mouthwash was assessed and it was concluded that none of the volunteers in the curcumin group experienced toxicity or reported any adverse outcomes, indicating that indicated clinically safe in adult (Santos Filho et al., 2018) as well as in children undergoing CT (Elad et al., 2013). Curcumin in doses of 500 mg thrice daily (1.5 g/day) reduced the incidence and severity of radiation-induced mucositis (Deodhar et al., 1980) and the safety of curcumin at up to 12 gm/day has been established (Anand et al., 2007; Eckert et al., 2017; Shehzad et al., 2010). To date, many clinical studies and some systematic reviews have been done, but none of the studies comprehensively synthesize the effectiveness of turmeric to alleviate OM. Thus, the purpose of this systematic review was to synthesize the effects of turmeric and curcumin in the management of OM induced by chemo and/or RT.

Methods

Study Design

This systematic review was conducted by the preferred reporting items for systematic reviews and meta-analysis guidelines (PRISMA) (Moher et al., 2009). No participants were involved in this study due to its nature as a systematic review; therefore, ethical committee approval was not required.

Inclusion Criteria

Included studies fulfilled the subsequent inclusion criteria: (1) The research design on the potential curcumin/turmeric therapeutic impact on RT/CT-induced OM utilized a RCT. (2) The subjects had to be 18 years or older. (3) The article was written and available in English. (4) Curcumin/turmeric was utilized to prevent or treat OM. (5) A placebo, chlorhexidine/povidone-iodine solution/normal saline mouthwash (NSS MW)/benzydamine, or another standardized intervention was administered to the control group (Table 1).

Exclusion Criteria

Studies where curcumin was administered in combination with other drugs and OM not associated with RT or CT were excluded. Review, commentary, editorial, and observational articles have not been included.

Search Strategy

The period covered by the review was September 2023–March 2024. Every reviewer independently searched the literature using six databases: Web of Science, Embase, Medline, Cochrane Library, CINHAL, and Embase. The search terms for the literature were Indian saffron, curcumin, and turmeric. Using the Boolean operations "OR" and "AND," HNC, head and neck neoplasm, and OM were employed singly or

Table 1.
PICOT Criteria of Included Studies

Population	Head and neck cancer patients scheduled to receive RT/CT or RCT
Intervention	Turmeric, curcumin, or Indian saffron formulations
Comparators	Placebo formulations, chlorhexidine/povidone-iodine solution, normal saline, benzydamine, or other standardized intervention
Outcome	Chemo/radiotherapy-induced mucositis and associated oral dysfunctions
Time	Published in last 10 year
Study design	Randomised and controlled trial

in combination. Without regard to a time restriction or deadline, a literature search was conducted. The reference list for each of the chosen papers was manually checked to identify any missing studies. Only works published and exclusively in English literature are included in the review search. The most current search date was May 23, 2023. The evaluation was conducted strictly to study the title and summary. The texts of the relevant articles matched the inclusion conditions after exclusion. After that, full texts of the pertinent articles were obtained. Disagreements among the articles were discussed and resolved.Treatment-induced mucositis was the main outcome, and secondary outcomes were oral dysfunction, treatment compliance, side effects of treatment, and weight loss. A narrative synthesis was created using the data from the selected trials, which included the characteristics of the intervention and control groups as well as the participants.

Data Extraction
Two reviewers (Reviewer 1 and Reviewer 2) proceeded with the screening process independently to find relevant papers based on eligibility criteria. The publications' entire texts and abstracts were chosen for review after the titles had first been checked. Before being included in the evaluation, studies had to pass screening by verifying eligibility criteria. Independent data retrieval from the eligible articles was done by the first two reviewers (Reviewers 1 and 2), and this was later confirmed by Reviewer 3. Each reviewer individually examined the table before discussing it with one another to reach a decision and prevent biases. Following the extraction of data from every article, data was entered into a table that includes the author, the year, the country, the sample size and details, the type of treatment (radiation, CT, or both), the characteristics of the intervention, the formulation of curcumin with its dosage and frequency, the outcome variables, grading scales that were utilized, and the study's conclusion (Table 2).

Quality Assessment
Cochrane Risk of Bias was relied upon to evaluate the bias risk of the included studies (Higgins et al., 2011). The risk areas included the completeness of data (attrition bias), concealment of selection and randomization (both in selection bias), blindness of patients and staff (performance bias), blindness of outcome assessors (detection bias), and biased reporting of data (reporting bias) (Table 3, Figure 1). In the event of any disputes, the reviewers resolved the biases of the included studies through independent evaluation and consultation with additional reviewers. Three grades were used for grading bias: low, high, and unclear risk of bias. It was deemed ambiguous or unclear when key criteria were absent or had insufficient information in the study.

Results

Figure 2 shows a selection and retrieval process of eligible studies. A total of 406 studies were selected initially. Of these, 248 were duplicates, 4 study reports were unavailable, 24 studies were found ineligible, and 78 studies were excluded due to the title and abstract review. Fifty-two studies were analyzed for eligibility before the screening process, and a total of 14 RCTs were included in the systematic review.

Study Characteristics
All the included studies were from 2014 to 2023. The areas of origin were from three countries: India, Iran, and Thailand, as shown in the table. The duration of the examination varied from 2 to 8 weeks. The review comprised a range of 20 to 80 people in the included studies. Overall, 894 patients with HNC receiving RT/RCT were included in this systematic review. In studies (Arun et al., 2020; Charantimath, 2016; Kia et al., 2021; Patil et al., 2015; Rao et al., 2014; Rongmuang et al., 2023; Soni et al., 2022) patients underwent radio-chemotherapy, and studies (David, 2019; Delavarian et al., 2019; Jyothi, 2021; Mansourian et al., 2015; Ramezani et al., 2023; Shah et al., 2020; Thomas et al., 2023) underwent RT only.

Risk of Bias and Study Quality
Table 3, Figure 3 indicate an included study's risk of bias. Out of 14 studies randomization (Arun et al., 2020; Delavarian et al., 2019; Kia et al., 2021; Mansourian et al., 2015; Ramezani et al., 2023; Rongmuang et al., 2023; Shah et al., 2020; Soni et al., 2022; Thomas et al., 2023), concealment of selection, (Arun et al., 2020; Delavarian et al., 2019; Kia et al., 2021; Mansourian et al., 2015; Rao et al., 2014; Rongmuang et al., 2023; Shah et al., 2020; Thomas et al., 2023), and blinding of patients and staff (Arun et al., 2020; Delavarian et al., 2019; Kia et al., 2021; Mansourian et al., 2015; Ramezani et al., 2023; Shah et al., 2020; Soni et al., 2022) were done. Selective reporting was found in two studies (David, 2019; Jyothi, 2021) and attrition bias, i.e., participants dropping out during the study period, was also reported by the other two studies (Ramezani et al., 2023; Shah et al., 2020). However, the rate of missing data was not enough to bias results from a potential effect. Allocation concealment was not sufficient to prevent the risk of bias in some studies (Patil et al., 2015; Rao et al., 2014; Rongmuang et al., 2023; Thomas et al., 2023), and performance biases were present because both participants and staff were not blinded for assigned intervention, therefore,

Table 2.
Characteristics of Included Studies (n = 14)

Author	Year	Country	Treatment Type	Patients' Details Sex/ Age	Sample Size	Intervention	Therapy Duration, Dosage and Direction	Outcome Variables and Scales	Grading Scale	Results
Rao et al.	2014	India	RT/CRT	26-85 years, Women: 16, Men: 64. Mean: 55.96 ± 12.25)	80 (Group first: 40; Group second: 40)	Experimental group: Turmeric mouthwash; Control group: Povidone-iodine mouthwash (1:100)	Povidone-iodine gargles: 10 mL twice/ day × 6 weeks Turmeric gargles: 10 mL, 6 times/ day × 6 weeks	RIOM	RTOG	Turmeric gargles significantly delayed and reduced the severity of OM. Decreased intolerable Mucositis ($p < .0001$) and weight loss were significantly less ($p < .001$) in the turmeric group cohort. Lesser incidence of treatment breaks before 4 weeks ($p < .01$).
Patil et al.	2015	India	CRT	Experimental group: 39–70 years (Mean = 60) Control group: 40–71 years (Mean = 59) Male: 11, female: 09	20 (Intervention: 10; Control: 10)	Experimental group: Curcumin mouth rinse (0.004%); Control group: Chlorhexidine mouthwash (0.2%)	3 times/day × 20 days	Oral mucositis, erythema, ulceration, pain score	NRS, OMAS, and WHO	There was a statistically significant difference in the NRS ($p = .000$), erythema ($p = .050$), ulceration ($p = .000$), and WHO scores ($p = .003$) between the two groups. Oral candida infection was observed in the control group; no such adverse events were noticed in the experimental group, thus providing evidence in support of curcumin's efficacy and safety.
Mansourian et al.	2015	Iran	RT	Age (Mean): (Experimental group: 47.3 ± 9.7; Control group: 55.6 ± 14.6) Males: 31; Females: 06	37 (Experimental group: 19; Control group: 18)	Experimental group: Curcuma longa gel; Control group: Placebo topical gel	Topical application 3 times/day × 8 weeks	Oral mucositis	WHO, VAS	There was a significant difference in the frequency of different grades of mucositis, erythema, and ulcers in between groups ($p < .001$).
Charantimath et al.	2016	India	RCT	Males: 37; Females: 3	40 (Experimental group: 20; Control group: 20)	Experimental group: Cure Next gel; Control group: Chlorhexidine gluconate gel (1.0%)	3 times/day × 2 weeks	Oral mucositis	NRS, OMAS, WHO mucositis scale	Significant changes were seen in erythema ($p = .0003$), ulcer sizes ($p = .0010$), and mucositis score in first week ($p = .0004$) and second week ($p = .018$) between the groups.
Delavarian et. al.	2018	Iran	RT	Mean (Experimental group: 62.18 ± 15.07; Control group: 55.87 ± 15.33) Females: 13; Males: 19	32 (Experimental group: 16, Control: 16)	Experimental group: Nanocurcumin; Control group: Placebo tablets Containing lactose	Oral sina-curcumin 80 mg/day× 6 weeks	Oral mucositis	NCI-CTC v.2,	A statistically significant difference in the grading of OM between the two groups at all visits (weeks 1, 2, 3, 4, 5, 6) ($p < 0.05$).

David et al.	2019	India	RT	-	60 (Experimental: 30, Control: 30)	Experimental: Turmeric mouthwash; Control: sodium bicarbonate mouthwash	50 mL, 2 times/day × 1 week	Oral mucositis	NCI-CTC	Turmeric mouthwash showed significant ($p = .001$) reduced severity of OM as compared to the control group (sodium bicarbonate).
Soni et al.	2020	India	CRT	Mean age (Trial arm A:40; B arm: 46; C arm: 45) Males: 55 Females: 5	60 (20 in each arm)	Arm A: 1 gm/day BTF; Arm B: 1.5 gm/day; Arm C: Placebo capsules	Arm A: 2 times/day; Arm B: 3 times/day; Arm C: 3 times/day	RCTIOM, and severity of dysphagia, oral pain, dermatitis, weight loss, and treatment compliance	NCI-CTC	There were significant differences seen in mucositis severity (between A and C: $p = .011$; B and C: $p = .004$), oral pain (between arm A and arm C: $p = .027$; between arm B and C: $p = .011$), dysphagia (between arm A and arm C: $p = .025$, between arm B and C: $p = .010$) and dermatitis (only between arms B and C: $p = .037$) were seen in the turmeric group as compared to the control group.
Arun et al.	2020	India	RCT	30–90 years; Male: 28; Female: 33	Group first: 30 Group second : 31	Experimental group: Turmeric extract capsules; Control group: Placebo capsules	3 times/day (500 mg)	RIOM	WHO, NCI, CTCAE	There were similar grades of mucositis in the first 2 weeks of treatment, but a statistically significant difference was found from the third week onwards ($p < .0001$).
Kia et al.	2021	Iran	RT and CT	Mean age: 55.96 ± 1.10; Males: 28; Females: 22	Experimental group: 25; Control group: 25; Males: 28 Females: 22 Mean age: 55.96 ± 1.10	Experimental group: 80 mg Sina-curcumin; Control group: Placebo capsule	2 times/day × 7 weeks	Oral mucositis, Pain	WHO oral mucositis scale, NRS	The severity of OM was statistically significant in the experimental group than in the control group in weeks: first ($p = .010$), fourth ($p = .022$), and seventh week ($p < .001$). The pain score was lower in the study group than in the control group in seventh week ($p = .001$).
Shah et al.	2021	India	RT	Age: 26–96 years; Mean age: 554.34 ± 13.78; Male: 54, Females: 14	68 (Intervention: 35, control: 33)	Experimental group: Curcumin mouthwash (0.1%) Control group: benzydamine mouthwash (o.15%)	10 mL 3 times/day × 7 days	RIOM	WHO mucositis scale	Both types of mouthwash were effective in delaying the onset and preventing severe RIOM. The use of 0.1% curcumin mouthwash was able to delay the onset of RIOM significantly.
Jyothi et al.	2021	India	RT	Male: 42, female: 8	50 (Experimental: 25, Control: 25)	Experimental group: Turmeric mouthwash Control group: routine oral care	TMW: 50 mL for 30 seconds	Oral mucositis	WHO Oral Mucositis Grading Scale	There is a significant difference in the severity of oral mucositis between experimental and control groups ($p < .005$).

(*Continued*)

Table 2.
Characteristics of Included Studies (n = 14) (Continued)

Author	Year	Country	Treatment Type	Patients' Details Sex/ Age	Sample Size	Intervention	Therapy Duration, Dosage and Direction	Outcome Variables and Scales	Grading Scale	Results
Thomas et al.	2022	India	RT	Experimental group: 56.97 ± 12.72 (Male: 33, female: 13) Control Group: 58.261 ± 10.50 (Male: 36, female: 10)	92 (Intervention: 46, control: 46)	Experimental group: Turmeric mouthwash Control group: benzydamine mouthwash	10 mL, 6 times/day	Oral health status, Oral mucositis, Oral dysfunctions	OHAT, WHO Oral Toxicity Scale, PROMS, XSFI	Turmeric mouth was found to be effective in reducing the onset and severity of oral mucositis ($p = .001$), oral health status ($p = .001$), and oral dysfunctions ($p = .001$) in the experimental group.
Rongmuang et al.	2023	Thailand	CRT	Experimental group mean: 57 ± 9.8 Control group: 60 ± 9.1	23 (Experimental group: 10, Control group: 13)	Experimental group: Curcumin mouthwash in coconut solvent. Control group: Normal saline solution mouthwash	15 mL, 4 times/day	Oral mucositis, pain score, compliance	WHO Oral Mucositis Grading Scale, NRS, self-recorded book	However, the incidence of OM and pain ($p = .163$) were reduced in the curcumin group but the results were not significant, whereas the severity of oral mucositis was significantly reduced in the curcumin MW group ($p = .016$).
Ramezani et al.	2023	Iran	RT	Male: 23, female: 14. Mean age: 53.36	37 (Experimental first: 13, Experimental second: 12, Control group: 12	Experimental group first: Curcumin mouthwash (0.1% w/v) Experimental group second: Topical Sinacurcumin soft gel (40 mg) Control group: Placebo mouthwash	10 mL freshly prepared mouthwash 3 times/d or one capsule of Sinacurcumin 40 mg once/ day × 21 days	OM and related burning/pain	WHO Scale NRS	Patients treated with either oral or topical curcumin showed a significantly reduced severity and burning related to OM during the first 3 weeks after administration ($p < .001$) as compared to the control group.

Note: BTF = Bio-enhanced turmeric formulation; CRTIOM = Chemo-radiotherapy induced oral mucositis; NCI-CTC = National Cancer Institute-common toxicity criteria; NCI-CTCAE = National Cancer Institute Common Terminology Criteria for Adverse Events; NRS = Numerical rating scale; OHAT = Oral health assessment tool; OMAS = Oral mucositis assessment scale; PROMS = Patient-reported oral mucositis symptom scale; RIOM = Radiation-induced oral mucositis; RTOG = Radiation therapy oncology group; TMW/CMW = Turmeric/ Curcumin mouthwash; VAS = Visual analogue scale; XSFI = Xerostomia short-form inventory.

Table 3.
Risk of Bias Assessment

Articles	Random Sequence Generation	Allocation Concealment	Blinding of Participant and Personnel	Blinding of Outcome Assessment	Incomplete Outcome Data	Selective Reporting Bias	Other Bias	Total Score
Rao et al. (2014)	Unclear	Low risk	High risk	Low risk	Low risk	Low risk	Unclear	4/7
Patil et al. (2015)	Unclear	Unclear	High risk	High risk	Low risk	Low risk	Unclear	2/7
Mansourian et al. (2015)	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	5/7
Charantimath et al. (2016)	Unclear	Unclear	Unclear	Unclear	Low risk	Low risk	Unclear	2/7
Delavarian et al. (2019)	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	5/7
David et al. (2019)	Unclear	Unclear	Unclear	Unclear	Unclear	High risk	Unclear	0/7
Soni et al. (2021)	Low risk	Unclear	Low risk	Low risk	Low risk	Low risk	Unclear	6/7
Arun et al. (2020)	Low risk	Low risk	Low risk	High risk	Low risk	Low risk	Unclear	5/7
Kia et al. (2021)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Unclear	6/7
Shah et al. (2020)	Low risk	Low risk	Low risk	Unclear	High risk	Low risk	Unclear	4/7
Jyothi et al. (2021)	Unclear	Unclear	Unclear	Unclear	Unclear	High risk	Unclear	0/7
Thomas et al. (2023)	Low risk	Low risk	High Risk	High Risk	Low risk	Low risk	Unclear	4/7
Rongmuang et al. (2023)	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	Unclear	5/7
Ramezani et al. (2023)	Low risk	Unclear	Low risk	Low risk	High risk	Low risk	Unclear	3/7

those parts had a high risk. In studies (Kia et al., 2021; Ramezani et al., 2023; Rao et al., 2014; Rongmuang et al., 2023; Soni et al., 2022) the result assessors were adequately blinded by keeping the knowledge of the allocated intervention blinded to assessors. The process that was employed to produce randomization sequences was a computer-generated list/number/table (Delavarian et al., 2019; Ramezani et al., 2023; Rongmuang et al., 2023; Shah et al., 2020; Soni et al., 2022; Thomas et al., 2023), a block randomization method using computer-generated random numbers (Kia et al., 2021; Mansourian et al., 2015) and a 4x4 block randomisation. (Arun et al., 2020) It is not described how random numbers were generated in the studies (Charantimath, 2016; David, 2019; Jyothi, 2021; Patil et al., 2015; Rao et al., 2014). Randomization concealment was carried out with sealed envelopes in studies (Rao et al., 2014; Rongmuang et al., 2023; Thomas et al., 2023), identical packages (Delavarian et al., 2019; Kia et al., 2021; Mansourian et al., 2015; Shah et al., 2020), and sequentially numbered containers (Arun et al., 2020). Allocation concealment

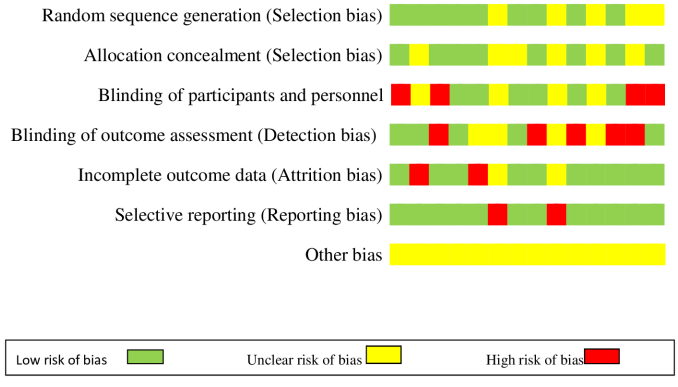

Figure 1.
Risk of Bias Graph.

was unclear (Charantimath, 2016; David, 2019; Jyothi, 2021; Patil et al., 2015; Ramezani et al., 2023; Soni et al., 2022).

Interventional Group Characteristics

The 14 included studies assessed various Curcumin medication formulations. Curcumin gel was used by two studies (Charantimath, 2016; Mansourian et al., 2015), Curcumin mouth rinse 0.004% (David, 2019; Jyothi, 2021; Patil et al., 2015; Ramezani et al., 2023; Rao et al., 2014; Rongmuang et al., 2023; Shah et al., 2020; Thomas et al., 2023), Nanocurcumin (Delavarian et al., 2019), Turmeric extract capsule (Arun et al., 2020), sina-curcumin (Kia et al., 2021; Ramezani et al., 2023), Bio-enhanced turmeric formulation (BTF) (Soni et al., 2022). Two studies (Ramezani et al., 2023; Soni et al., 2022) divided participants into three group arms, in the study (Ramezani et al., 2023) two arms contained different formulations of curcumin (one was turmeric mouthwash 0.1% w/v, and the other arm contained curcumin nanocapsules), while the other study used BTF capsules 1 g/day in one arm and 1.5 g/day in another arm.

Control Group Characteristics

Agent in the control group exhibited variation in the following forms: chlorhexidine gel (Charantimath, 2016), placebo topical gel (Mansourian et al., 2015), chlorhexidine mouthwash (Patil et al., 2015), povidone Iodine (Rao et al., 2014), placebo tablets-lactose (Delavarian et al., 2019), placebo capsules (Arun et al., 2020; Kia et al., 2021; Soni et al., 2022), saline mouthwash (Rongmuang et al., 2023), routine oral care (Jyothi, 2021), benzydamine mouthwash (Shah et al., 2020; Thomas et al., 2023), placebo mouthwash (Ramezani et al., 2023), and sodium bicarbonate mouthwash (David, 2019).

Measurement Tool

The most commonly utilized tools in selected articles are given in Table 2. It should be taken into account that no suggestion

regarding the superiority of one scale over another can be made based on evidence.

Turmeric Contains Vs. Conventional Therapy/Standard Care
The details of the comparison are as follows:

Effect on the Onset of Chemo/Radiotherapy-Induced Oral Mucositis
Out of 14 included studies 10 studies reported the onset of OM. Out of 10, 8 studies reported a lower occurrence of OM in the turmeric group, whereas two studies (Mansourian et al., 2015; Rongmuang et al., 2023) found a statistically non-significant difference between control and intervention. In this line, a study (Arun et al., 2020) presented a similar time of appearance of OM in the first 2 weeks from the treatment start in both groups but increased severity over time in the control group arm, including four severe cases of grade 3 mucositis by week 4. In contrast, patients in group A (73.3%) experienced grade 1 mucositis after 4 weeks of treatment. A statistical difference became apparent in the third week and onward ($p < .001$). The included studies (Delavarian et al., 2019; Mansourian et al., 2015; Rongmuang et al., 2023) showed a delay in OM initiation. One study (Delavarian et al., 2019) found that in the control group, OM developed sooner compared to the experimental group ($p = .002$), whereas a study (Rongmuang et al., 2023) discovered an inclination to a lower rate of OM in the curcumin group compared to NSS MW, and another reported (Jyothi, 2021) reported a diminution in OM after using turmeric (0.24 ± 1.2). A study (Shah et al., 2020) indicated that both types of mouthwash (Turmeric and Benzydamine) could not completely prevent the incidence or progression of OM ($p = .206$) reflecting equal weightage of both mouthwashes. Participants were divided into three arms: Arm A—BTF 1 gm/day, arm B—BTF 1.5 g/day, and Arm C (placebo arm)—results showed that the occurrence of OM was lower in both arms (A and B) as compared to the placebo (Soni et al., 2022).

Effect on the Severity of Chemo/Radiotherapy-Induced Oral Mucositis
All included studies (Arun et al., 2020; Charantimath, 2016; David, 2019; Delavarian et al., 2019; Jyothi, 2021; Kia et al., 2021; Mansourian et al., 2015; Patil et al., 2015; Ramezani et al., 2023; Rao et al., 2014; Rongmuang et al., 2023; Shah et al., 2020; Soni et al., 2022; Thomas et al., 2023) assessed the turmeric/turmeric effects on the severity of therapy-induced OM (TIOM), and 13 studies reported a decreased severity of TIOM among the turmeric group, whereas one reported (Rongmuang et al., 2023) non-significant results among the experimental

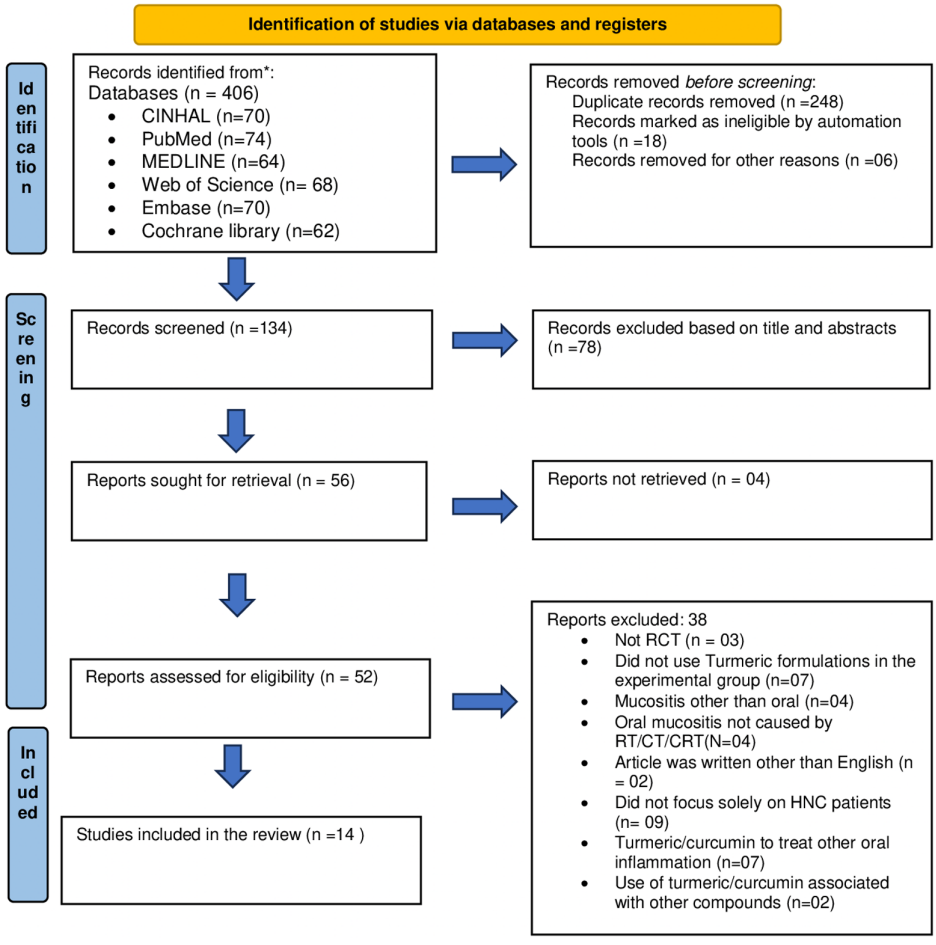

Figure 2.
Selection and Retrieval Process of Eligible Studies.

and control groups. A study (Delavarian et al., 2019) suggested that although TIOM gradually worsened in both groups, but was less severe than in the control group of mucositis ($p < .05$). Also, no patients in the research group had grade 4 mucositis compared to 50% of the control group. Comparing Turmeric vs. Chlorhexidine, two studies (Charantimath, 2016; Patil et al., 2015) assessed turmeric compared with chlorhexidine in this respect, and both reported a significant reduction in the grading reduction of OM in the interventional group. Morbidity due to OM was also lower in the turmeric group as reported by the study with $p = .0001$ (Patil et al., 2015). A study (Shah et al., 2020) also found that none of the mouthwashes (Turmeric and benzydamine) completely prevented the progression of OM, so they concluded turmeric MW was equally effective as benzydamine MW in HNC patients in reducing the severity of OM. The study (Jyothi, 2021) also reported that although in the starting (fifth and tenth weeks of intervention) there were no significant differences in the mean mucositis score, the result was conclusive on the 15th day post-transplant. In comparison, a study (Kia et al., 2021) found a significant reduction in severity every week post-transplant (first week: $p = .010$, fourth week: $p = .022$, and seventh week: $p < 0.001$). Figure 4 indicates the mean scores for mucositis grade before and after using turmeric/curcumin or a control intervention.There was a noticeable reduction in the intensity of OM in the turmeric/curcumin group.

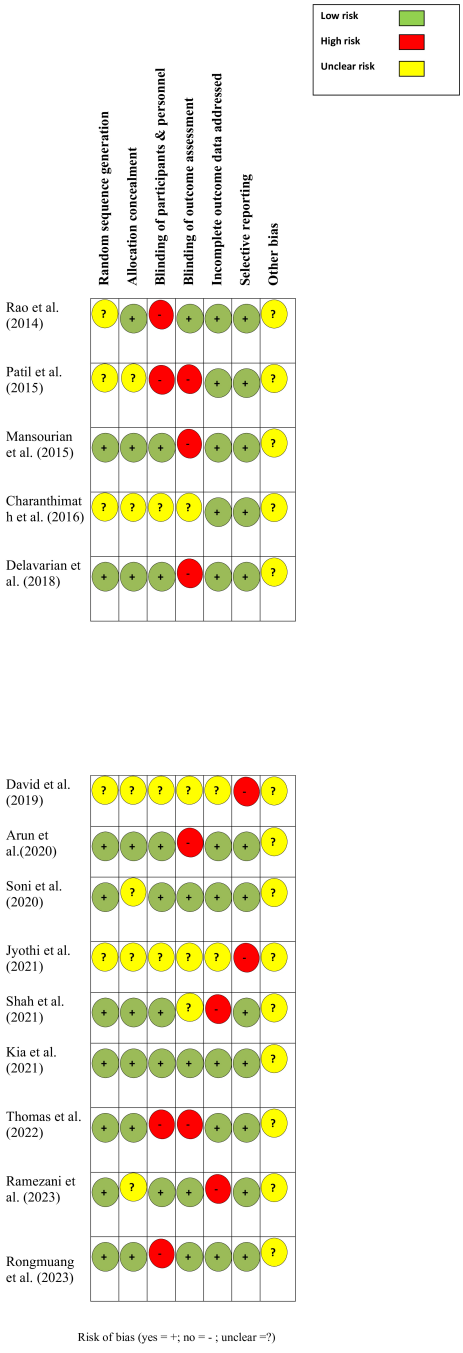

Figure 3.
Risk of bias (yes = +; no = - ; unclear = ?).

Improvement in Oral Dysfunction

In this section, the results regarding the effectiveness of turmeric formulations in reducing pain, dysphagia, xerostomia, erythema, ulceration, burning, alteration in taste, dermatitis, weight loss, oral candidiasis, and degree of oral function impairment caused by mouth ulcers, including speaking, swallowing, drinking, and eating, were synthesized from the included studies. Turmeric-reducing oral dysfunction is mentioned in eight research. Reduction in pain (Charantimath, 2016; Mansourian et al., 2015; Patil et al., 2015; Thomas et al., 2023), erythema (Charantimath, 2016; Mansourian et al., 2015; Patil et al., 2015), and ulceration size (Charantimath, 2016; Mansourian et al., 2015; Patil et al., 2015) were observed in various studies. Additionally, in the turmeric group, various studies reported a decrease in burning sensation (Mansourian et al., 2015), xerostomia scores, and difficulty in speaking, drinking, eating hard food, and swallowing were found in the study (Thomas et al., 2023). Studies observed that the groups using turmeric formulations had less incidence of dermatitis (Soni et al., 2022) and oral candidiasis (Patil et al., 2015; Rongmuang et al., 2023). Another study (Ramezani et al., 2023) notes that more than 33% of the patients using various formulations of turmeric experienced no ulcer recurrence, whereas all placebo recipients had OM.

Treatment Interruption Due to Chemo/Radiotherapy-Induced Oral Mucositis

Three studies (Rao et al., 2014; Soni et al., 2022; Thomas et al., 2023) reported it, and two of them found that the control group had more treatment interruptions due to the severity of OM. Among others that followed this path, one study (Thomas et al., 2023) showed fewer days of interruption for the experimental group (0.47 ± 1.40 days) compared to the control group (3 ± 3.04 days; $p = .002$). In another study (Soni et al., 2022) sequential interruption of RT was observed among 15% of patients in arm B (BTF 1.5 gm/day), 20% of patients (BTF-1 gm/day) in arm A ($p = .677$), and 55% of patients in arm C ($p = .008$). However, a study (Rao et al., 2014) revealed that compliance to treatment was better in the turmeric group than in the povidone-iodine as the number of treatment days lost was 7.25 ± 0.56 and 7 ± 00 respectively but it was statistically not significant between both groups.

Weight Loss

Body weight before and after CT/RT was outlined in 4 included studies. A study (Delavarian et al., 2019) showed that the adjusted average weight loss was 1.32 ± 0.87 kg in control

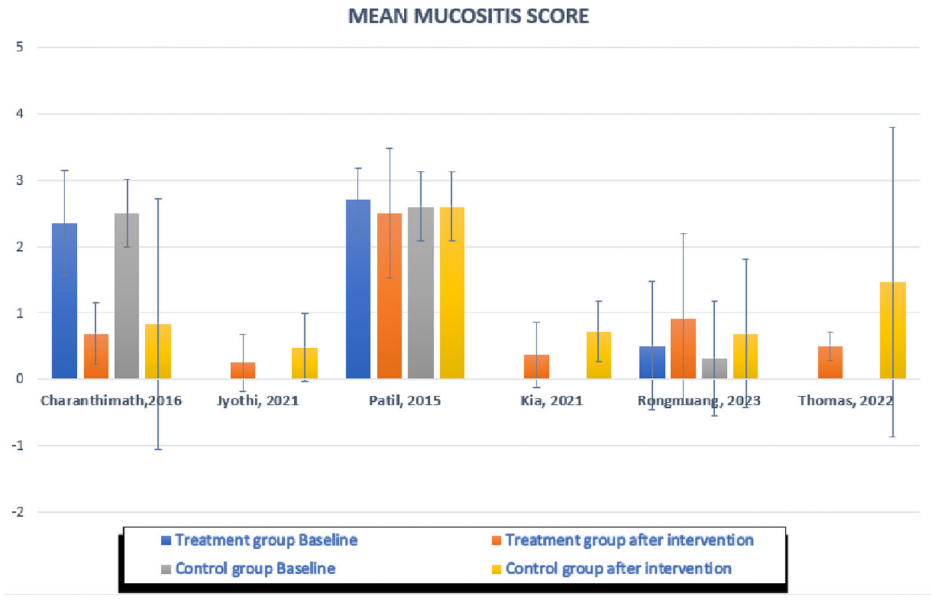

Figure 4.
Mean Mucositis Score and Standard Deviation in Both Groups Before and After Intervention (0 = No Mucositis to 4 = Severe Mucositis).

group participants vs. 0.43 ± 0.81 kg in experimental arm individuals, respectively. The change in body weight differed significantly between groups ($p = .003$). Significant differences in body weight were also observed in studies (Rao et al., 2014; Soni et al., 2022; Thomas et al., 2023). A study (Thomas et al., 2023) observed that at the end of therapy, significant weight loss was greater in the control group (from 58.95 ± 8.60 to 54 ± 8.74) than the experimental group ($p = .001$). While other trials (Rao et al., 2014) also found that weight loss was less in turmeric cohorts (3.92 ± 2.13) compared to the povidone-iodine group (4.45 ± 2.15). Patients using any form of turmeric were found to lose less weight, with a significant disparity ($p = .002$) in the control group as well (Soni et al., 2022).

Safety/Side Effects of Turmeric Intervention

Safety and side effects regarding the use of turmeric/curcumin have been reported by 8 included studies. Out of 8, six studies didn't report any side effects and concluded that turmeric is safe to use. However, in two studies (Mansourian et al., 2015; Shah et al., 2020) patients in the turmeric group reported nausea and burning sensations. In six studies (Arun et al., 2020; Charantimath, 2016; Delavarian et al., 2019; Mansourian et al., 2015; Patil et al., 2015; Rongmuang et al., 2023) there were no reports of patients in the curcumin group experiencing side effects or discomfort as a result of oral consumption. Two patients also had nausea in the study (Mansourian et al., 2015), while burning was reported by all participants in the study (Shah et al., 2020). Figure 5 shows the impact of turmeric/curcumin on secondary outcomes as reported in several research. The most common consequences were less weight loss, diminished ulcer size, and less pain.

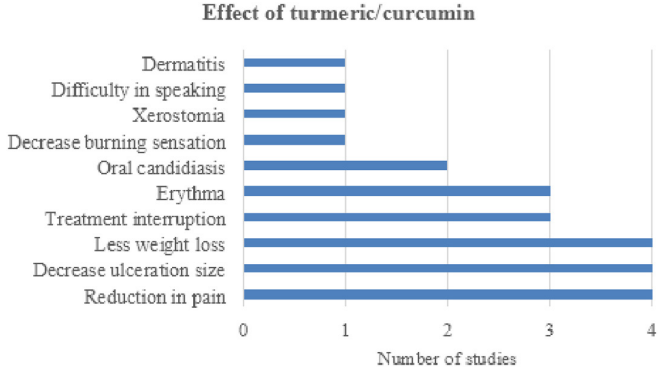

Figure 5.
Secondary Outcomes.

Discussion

Oral mucositis is inevitably a distressing complication caused by oral cancer therapy such as CT and RT, and it adversely affects oral function. One of the primary causes of CT and RT dosage limitations is OM, which also significantly decreases patient quality of life. Complications with cancer treatment-induced mucositis include burning, altered taste, xerostomia, ulceration, sloughing of tissue, and pain, as well as difficulties swallowing, speaking, drinking, and eating. All studies found the efficacy and safety of turmeric/curcumin formulations in preventing/treating mucositis due to treatment and other oral dysfunctions related to HNC. The included study findings were reviewed, and the conclusion is that curcumin delays significantly both the development (Arun et al., 2020; David, 2019; Delavarian et al., 2019; Jyothi, 2021; Rao et al., 2014; Shah et al., 2020; Soni et al., 2022; Thomas et al., 2023) as well as severe OM (Arun et al., 2020; Charantimath, 2016; David, 2019; Delavarian et al., 2019; Jyothi, 2021; Kia et al., 2021; Mansourian et al., 2015; Patil et al., 2015; Ramezani et al., 2023; Rao et al., 2014; Shah et al., 2020; Soni et al., 2022; Thomas et al., 2023). However, there was no statistically significant difference favoring the prevention of overall incidence or severity of OM.

Consistent results were also reported by a systematic review done by the study (Dharman et al., 2021) and concluded that all formulations of turmeric and curcumin are well-tolerated, safe, and effective at delaying the development and severity of OM and alleviating the symptoms of TIOM. Reduction of pain score, erythema, and decrease in onset and severity of OM were also observed in the turmeric group as reported by other systematic reviews (Normando et al., 2019; Rai et al., 2021) and consistent results were also found in the present review. In a study, pediatric patients undergoing CT used curcumin mouthwash to prevent the initiation of OM (Elad et al., 2013). They concluded that curcumin mouthwash was well-accepted and convenient. Among seven studies (David, 2019; Jyothi, 2021; Patil et al., 2015; Ramezani et al., 2023; Rao et al., 2014; Shah et al., 2020; Thomas et al., 2023) curcumin mouthwashes were used in the experimental group. This was presumably because it is easy to apply without necessitating the solution to be in more contact with the mucosa. Although all results were in favor of curcumin/turmeric mouthwashes, the concentrations of mouthwashes were different in the included studies. Moreover, two studies evaluating turmeric efficacy as a combination with honey to use for OM management reported lower OM scores in the treatment group post-solution application (Francis and Williams, 2014; Charalambous et al., 2018). However, both studies were omitted from the descriptive analysis of this systematic review. The advantage of honey as a solvent of curcumin is reported by studies (Hk et al., 2015; Xu et al., 2016). However, they didn't report on the concentration of curcumin ingredients. Toxicity is the main reason why some drugs cannot be used for OM treatment (Hk et al., 2015). Because curcumin is made from a natural plant extract, it is free of risks. In this direction, studies have proven the safety of curcumin (Elad et al., 2013; Saldanha, 2014; Verma, 2016). Rai et al. (Rai et al., 2021) observed that the group using turmeric formulation showed improvement in mouth opening and decreased burning sensation related to OM (Lalla et al., 2014). Turmeric administered topically as a mouthwash or gel is less costly, easier to apply, and less likely to cause side effects than systemic treatments, as shown by numerous studies (Charantimath, 2016; Mansourian et al., 2015). However, due to the limited bioavailability, and poor solubility and absorption of turmeric or curcumin when taken orally, to counteract this, the study (Delavarian et al., 2019) used oral curcumin in the form of nano-micelles (80 mg/day tablet), whereas another study (Rongmuang et al., 2023) contained coconut oil as a solvent for preparing turmeric mouthwash. Strengths included the rigorous evaluation of the included studies' quality using the Cochrane risk-of-bias method and its thorough literature search that involved both manual and numerous database searches. It is imperative to consider various methodological constraints associated with this review. First, the included studies' turmeric formulations showed significant heterogeneity, and the direction, intervention duration, and assessment criteria for mucositis were inconsistent, which rendered the meta-analysis impractical. Moreover, the majority of the studies lacked specific information regarding radiation and CT dosage.

Study Limitations

It is imperative to consider various methodological constraints associated with this review. First, the included studies' turmeric formulations showed significant heterogeneity, and the direction, intervention duration, and assessment criteria for mucositis were inconsistent, which rendered the meta-analysis impractical. Moreover, the majority of the studies lacked specific information regarding radiation and CT dosage. Optimal dosage and frequency of circumin to reduce the RIOM couldn't explored remained to be exploreed.

Conclusion and Recommendation

By reviewing the included studies, it has been concluded that turmeric formulations effectively delayed the onset and severity of TIOM. In addition, turmeric/curcumin formulations effectively reduced OM-related pain, erythema, burning, ulceration areas, and oral dysfunction. Turmeric formulations may be implemented as an adjuvant to supplement standard oral care. However, by reviewing these studies, it remains inconclusive regarding the exact doses and frequency of turmeric formulations required to prevent OM. As no study has yet determined the best frequency and duration of intervention, an issue to be solved in future studies is comparing different forms of turmeric (gel, mouthwash, capsules) with their most adequate dose per day. The long-term effects of turmeric on HNC patients should be studied. Nonetheless, high-quality, multi-centre, RCTs utilizing various formulations of turmeric and curcumin are required. Furthermore, the applicability of the turmeric formulation needs further research in terms of which type of patients (undergoing CT, RT, CRT) are more likely to benefit, and at what time during therapy intervention should be started to get maximum benefits. Some of these opportunities for future research are included in this review closely, with a focus on defining precisely the therapeutic dose of turmeric formulations mitigating OM occurrence and severity.

Data Availability Statement: The datasets used in this study are not publicly accessible; however, they can be obtained from the corresponding author upon reasonable request.

Peer-review: Externally peer-reviewed.

Author Contributions: Conception – P.D., U.P., N.K.; Design – P.D., A.R.; Supervision – N.K., U.P.; Funding – Nil; Materials – P.D., A.R., U.P.; Data Collection and/or Processing – P.D., N.K.; Analysis and/or Interpretation – P.D., U.P.; Literature Review – A.R., P.D.; Writing – P.D., U.P., A.R.; Critical Review – N.K., P.D., U.P., A.R.

Declaration of Interests: The authors declare that they have no competing interest.

Funding: The authors declared that this study has received no financial support.

References

Anand, P., Kunnumakkara, A. B., Newman, R. A., & Aggarwal, B. B. (2007). Bioavailability of curcumin: Problems and promises. *Molecular Pharmaceutics, 4*(6), 807–818. [CrossRef]

Anderson, C. M., Sonis, S. T., Lee, C. M., Adkins, D., Allen, B. G., Sun, W., Agarwala, S. S., Venigalla, M. L., Chen, Y., Zhen, W., Mould, D. R., Holmlund, J. T., Brill, J. M., & Buatti, J. M. (2018). Phase 1b/2a trial of the superoxide dismutase mimetic GC4419 to reduce

chemoradiotherapy-induced oral mucositis in patients with oral cavity or oropharyngeal carcinoma. *International Journal of Radiation Oncology, Biology, Physics*, *100*(2), 427–435. [CrossRef]

Arun, P., Sagayaraj, A., Azeem Mohiyuddin, S. M., & Santosh, D. (2020). Role of turmeric extract in minimising mucositis in patients receiving radiotherapy for head and neck squamous cell cancer: A randomised, placebo-controlled trial. *Journal of Laryngology and Otology*, *134*(2), 159–164. [CrossRef]

Bensinger, W., Schubert, M., Ang, K.-K., Brizel, D., Brown, E., Eilers, J. G., Elting, L., Mittal, B. B., Schattner, M. A., Spielberger, R., Treister, N. S., & Trotti, A. M. (2008). [NCCN Task Force report]. NCCN Task Force Report. Prevention and management of mucositis in cancer care. *Journal of the National Comprehensive Cancer Network: JNCCN*, *6* Suppl. 1, S1–S21; quiz S22–S24.

Borges, G. Á., Rêgo, D. F., Assad, D. X., Coletta, R. D., De Luca Canto, G., & Guerra, E. N. S. (2017). In vivo and in vitro effects of curcumin on head and neck carcinoma: A systematic review. *Journal of Oral Pathology and Medicine: Official Publication of the International Association of Oral Pathologists and the American Academy of Oral Pathology*, *46*(1), 3–20. [CrossRef]

Charantimath, S. (2016). *Use of curcumin in radiochemotherapy induced oral mucositis patients: A control trial study*.International Scholarly and Scientific Research & Innovation, 10(3), 147-152.[CrossRef]

David, R & Shree,T. (2019). Effectiveness of turmeric mouthwash and sodium bicarbonate mouthwash to reduce oral mucositis among patient undergoing radiation therapy. *Scholars international journal of traditional and complementary medicine*,*2*(7),124-127.

Delavarian, Z., Pakfetrat, A., Ghazi, A., Jaafari, M. R., Homaei Shandiz, F., Dalirsani, Z., Mohammadpour, A. H., & Rahimi, H. R. (2019). Oral administration of nanomicelle curcumin in the prevention of radiotherapy-induced mucositis in head and neck cancers. *Special Care in Dentistry: Official Publication of the American Association of Hospital Dentists, the Academy of Dentistry for the Handicapped, and the American Society for Geriatric Dentistry*, *39*(2), 166–172. [CrossRef]

Deodhar, S. D., Sethi, R., & Srimal, R. C. (1980). Preliminary study on antirheumatic activity of curcumin (diferuloyl methane). *Indian Journal of Medical Research*, *71*, 632–634.

Dharman, S., G, M., Shanmugasundaram, K., & Sampath, R. K. (2021). A systematic review and meta-analysis on the efficacy of curcumin/turmeric for the prevention and amelioration of radiotherapy/radiochemotherapy induced oral mucositis in head and neck cancer patients. *Asian Pacific Journal of Cancer Prevention: APJCP*, *22*(6), 1671–1684. [CrossRef]

Eckert, J., Scott, B., Lawrence, S. M., Ihnat, M., & Chaaban, H. (2017). FLLL32, a curcumin analog, ameliorates intestinal injury in necrotizing enterocolitis. *Journal of Inflammation Research*, *10*, 75–81. [CrossRef]

Elad, S., Meidan, I., Sellam, G., Simaan, S., Zeevi, I., Waldman, E., Weintraub, M., & Revel-Vilk, S. (2013). Topical curcumin for the prevention of oral mucositis in pediatric patients: Case series. *Alternative Therapies in Health and Medicine*, *19*(3), 21–24.

Francis, M., & Williams, S. (2014). Effectiveness of Indian turmeric powder with honey as complementary therapy on oral mucositis: A nursing perspective among cancer patients in Mysore. *Nursing Journal of India*, *105*(6), 258–260. [CrossRef]

Higgins, J. P. T., Altman, D. G., Gøtzsche, P. C., Jüni, P., Moher, D., Oxman, A. D., Savovic, J., Schulz, K. F., Weeks, L., Sterne, J. A. C., Cochrane Bias Methods Group, & Cochrane Statistical Methods Group (2011). The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*, *343*, d5928. [CrossRef]

Hk, C., Ym, J., Hs, L., Yj, L., & Sh, H. (2015). Effects of honey on oral mucositis in patients with head and neck cancer: A meta-analysis. *The Laryngoscope*, *125*(9). [CrossRef]

Kanagalingam, J., Chopra, A., Hong, M. H., Ibrahim, W., Villalon, A., & Lin, J.-C. (2017). Povidone-iodine for the management of oral mucositis during cancer therapy. *Oncology Reviews*, *11*(2), 341. [CrossRef]

Kia, S. J., Basirat, M., Saedi, H. S., & Arab, S. A. (2021). Effects of nanomicelle curcumin capsules on prevention and treatment of oral mucosits in patients under chemotherapy with or without head and neck radiotherapy: A randomized clinical trial. *BMC Complementary Medicine and Therapies*, *21*(1), 232. [CrossRef]

Lalla, R. V., Saunders, D. P., & Peterson, D. E. (2014). Chemotherapy or radiation-induced oral mucositis. *Dental Clinics of North America*, *58*(2), 341–349. [CrossRef]

Liczbiński, P., Michałowicz, J., & Bukowska, B. (2020). Molecular mechanism of curcumin action in signaling pathways: Review of the latest research. *Phytotherapy Research*, *34*(8), 1992–2005. [CrossRef]

Lüer, S. C., Goette, J., Troller, R., & Aebi, C. (2014). Synthetic versus natural curcumin: Bioequivalence in an in vitro oral mucositis model. *BMC Complementary and Alternative Medicine*, *14*, 53. [CrossRef]

Charalambous, M., Raftopoulos, V., Paikousis, L., Katodritis, N., Lambrinou, E., Vomvas, D., Georgiou, M., Charalambous, A. (2018). The effect of the use of thyme honey in minimizing radiation - induced oral mucositis in head and neck cancer patients: A randomized controlled trial. *European Journal of Oncology Nursing : The Official Journal of European Oncology Nursing Society*, *34*, 89–97. [CrossRef]

Jyothi, N. M., U B, V., & S Natekar, D. (2021). A randomized clinical trial to assess the effectiveness of turmeric mouth Wash on radiation induced oral mucositis among patient with head and neck cancer admitted at oncology units of selected hospitals of Bagalkot. *International Journal of Science and Research*, *10*(12), 607–610. [CrossRef]

Mansourian, A., Amanlou, M., Shirazian, S., Jahromi, Z., & Amirian, A. (2015). The effect of "Curcuma longa" topical gel on radiation-induced oral mucositis in patients with head and neck cancer. *International Journal of Radiaton Research*, *13*(3), 269–274. [CrossRef]

Manzi, N. de M., Silveira, R. C. de C. P., & dos Reis, P. E. D. (2016). Prophylaxis for mucositis induced by ambulatory chemotherapy: Systematic review. *Journal of Advanced Nursing*, *72*(4), 735–746. [CrossRef]

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA statement. *PLoS Medicine*, *6*(7), e1000097. [CrossRef]

Nabavi, S. M., Russo, G. L., Tedesco, I., Daglia, M., Orhan, I. E., Nabavi, S. F., Bishayee, A., Nagulapalli Venkata, K. C., Abdollahi, M., & Hajheydari, Z. (2018). Curcumin and melanoma: From chemistry to medicine. *Nutrition and Cancer*, *70*(2), 164–175. [CrossRef]

Normando, A. G. C., de Menêses, A. G., de Toledo, I. P., Borges, G. Á., de Lima, C. L., dos Reis, P. E. D., & Guerra, E. N. S. (2019). Effects of turmeric and curcumin on oral mucositis: A systematic review. *Phytotherapy Research*, *33*(5), 1318–1329. [CrossRef]

Palatty, P. L., Azmidah, A., Rao, S., Jayachander, D., Thilakchand, K. R., Rai, M. P., Haniadka, R., Simon, P., Ravi, R., Jimmy, R., D'souza, P. F., Fayad, R., & Baliga, M. S. (2014). Topical application of a sandal wood oil and turmeric based cream prevents radiodermatitis in head and neck cancer patients undergoing external beam radiotherapy: A pilot study. *British Journal of Radiology*, *87*(1038), 20130490. [CrossRef]

Patil, K., Guledgud, M. V., Kulkarni, P. K., Keshari, D., & Tayal, S. (2015). Use of curcumin mouthrinse in radio-chemotherapy induced oral mucositis patients: A pilot study. *Journal of Clinical and Diagnostic Research*, *9*(8), ZC59–ZC62. [CrossRef]

Rai, A., Kumar, N., Sharma, S., Parveen, S., & Rasheed, A. (2021). Turmeric in the management of oral submucous fibrosis: A systematic review and meta-analysis. *Journal of Cancer Research and Therapeutics*, *17*(2), 327–335. [CrossRef]

Ramezani, V., Ghadirian, S., Shabani, M., Boroumand, M. A., Daneshvar, R., & Saghafi, F. (2023). Efficacy of curcumin for amelioration of radiotherapy-induced oral mucositis: A preliminary randomized controlled clinical trial. *BMC Cancer*, *23*(1), 354. [CrossRef]

Rao, S., Dinkar, C., Vaishnav, L. K., Rao, P., Rai, M. P., Fayad, R., & Baliga, M. S. (2014). The Indian spice turmeric delays and mitigates radiation-induced oral mucositis in patients undergoing treatment for head and neck cancer: An investigational study. *Integrative Cancer Therapies*, *13*(3), 201–210. [CrossRef]

Ribeiro da Silva, V. C., da Motta Silveira, F. M., Barbosa Monteiro, M. G., da Cruz, M. M. D., Caldas Júnior, A. de F., & Pina Godoy, G. (2018). Photodynamic therapy for treatment of oral mucositis: Pilot study with pediatric patients undergoing chemotherapy. *Photodiagnosis and Photodynamic Therapy*, *21*, 115–120. [CrossRef]

Rongmuang, J., Sunpaweravong, P., Dechaphunkul, A., Tangthongkum, M., Puttarak, P., Prisutkul, A., & Sathitruangsak, C. (2023). The efficacy of curcumin mouthwash in coconut oil solvent for preventing oral mucositis in locally advanced head and neck cancer patients undergoing concurrent chemoradiotherapy. *International Journal of Cancer Research & Therapy*, *8*(2), 34–45.

Ryan, J. L., Heckler, C. E., Ling, M., Katz, A., Williams, J. P., Pentland, A. P., & Morrow, G. R. (2013). Curcumin for radiation dermatitis: A randomized, double-blind, placebo-controlled clinical trial of thirty breast cancer patients. *Radiation Research*, *180*(1), 34–43. [CrossRef]

Saldanha, S. P. (2014). A Comparative study to assess the effectiveness of turmeric mouth wash versus saline mouth wash on treatment induced oral mucositis (Tiom) in a selected hospital at Mangalore. *Journal of Clinical Research and Bioethics*, *5*(6). [CrossRef]

Santos Filho, E. X. D., Arantes, D. A. C., Oton Leite, A. F., Batista, A. C., Mendonça, E. F. de, Marreto, R. N., Naves, L. N., Lima, E. M., & Valadares, M. C. (2018). Randomized clinical trial of a mucoadhesive formulation containing curcuminoids (Zingiberaceae) and Bidens pilosa Linn (Asteraceae) extract (FITOPROT) for prevention and treatment of oral mucositis—Phase I study. *Chemico-Biological Interactions*, *291*, 228–236. [CrossRef]

Scully, C., Epstein, J., & Sonis, S. (2003). Oral mucositis: A challenging complication of radiotherapy, chemotherapy, and radiochemotherapy: part 1, pathogenesis and prophylaxis of mucositis. *Head and Neck*, *25*(12), 1057–1070. [CrossRef]

Shah, S., Rath, H., Sharma, G., Senapati, S. N., & Mishra, E. (2020). Effectiveness of curcumin mouthwash on radiation-induced oral mucositis among head and neck cancer patients: A triple-blind, pilot randomised controlled trial. *Indian Journal of Dental Research: Official Publication of Indian Society for Dental Research*, *31*(5), 718–727. [CrossRef]

Shehzad, A., Khan, S., Shehzad, O., & Lee, Y. S. (2010). Curcumin therapeutic promises and bioavailability in colorectal cancer. *Drugs of Today*, *46*(7), 523–532. [CrossRef]

Soni, T. P., Gupta, A. K., Sharma, L. M., Singhal, H., Sharma, S., & Gothwal, R. S. (2022). A randomized, placebo-controlled study to evaluate the effect of bio-enhanced turmeric formulation on radiation-induced oral mucositis. *ORL; Journal for Oto-Rhino-Laryngology and Its Related Specialties*, *84*(2), 103–113. [CrossRef]

Sonis, S. T. (2004). The pathobiology of mucositis. *Nature Reviews. Cancer*, *4*(4), 277–284. [CrossRef]

Thomas, P. L., Kang, H. K., & Rishi, K. S. (2023). Randomized control study of the effects of turmeric mouthwash on Oral Health status, treatment-induced mucositis, and associated oral dysfunctions among patients with head and neck cancer. *Cancer Nursing*, *46*(1), 36–44. [CrossRef]

Trotti, A., Bellm, L. A., Epstein, J. B., Frame, D., Fuchs, H. J., Gwede, C. K., Komaroff, E., Nalysnyk, L., & Zilberberg, M. D. (2003). Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: A systematic literature review. *Radiotherapy and Oncology: Journal of the European Society for Therapeutic Radiology and Oncology*, *66*(3), 253–262. [CrossRef]

Vaughn, A. R., Branum, A., & Sivamani, R. K. (2016). Effects of turmeric (Curcuma longa) on skin health: A systematic review of the clinical evidence. *Phytotherapy Research: PTR*, *30*(8), 1243–1264. [CrossRef]

Verma, V. (2016). Relationship and interactions of curcumin with radiation therapy. *World Journal of Clinical Oncology*, *7*(3), 275–283. [CrossRef]

Xu, J. L., Xia, R., Sun, Z. H., Sun, L., Min, X., Liu, C., Zhang, H., & Zhu, Y. M. (2016). Effects of honey use on the management of radio/chemotherapy-induced mucositis: A meta-analysis of randomized controlled trials. *International Journal of Oral and Maxillofacial Surgery*, *45*(12), 1618–1625. [CrossRef]