

A Systematic Review on the Efficacy of Supersaturated Calcium Phosphate in the Management of Head and Neck Cancer Patients

Anwesha Mishra, BDS, Gunjan Kumar, MDS, Ph.D., Ipseeta Menon, MDS, Ph.D.,
Kunal Jha, MDS, Ph.D., Arpita Singh, MDS, Ph.D., Kabir Suman Dash, MDS

Department of Public Health Dentistry, Kalinga Institute of Dental Sciences (KIDS), Kalinga Institute of Industrial Technology (KIIT)
Deemed to be University, Bhubaneswar, Odisha, India.

Received 4 October 2025 • Revised 4 February 2026 • Accepted 8 February 2026 • Published online 29 September 2026

Abstract:

Objective: This systematic review assessed the effectiveness of supersaturated calcium phosphate in treating patients with head and neck cancer.

Material and Methods: In accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines, a structured search was developed using the Participants, Intervention, Comparison, Outcomes (PICO) framework. This search was conducted across four electronic databases: PubMed, EMBASE, Web of Science, and Scopus, along with an additional search in Google Scholar. Data extraction and risk of bias evaluation were carried out by two independent reviewers utilizing the National Institutes of Health (NIH) assessment tool.

Results: Among the 95 studies, 9 were selected for inclusion in the systematic review. The quality of these studies was evaluated using the NIH assessment tool. Among the included studies, 5 reported a beneficial effect in reducing oral mucositis following the use of supersaturated calcium phosphate, while 4 found no significant impact on mucositis from its use.

Conclusion: All the available research consistently indicates that supersaturated calcium phosphate effectively decreases the frequency, length, and intensity of oral mucositis in individuals with head and neck cancer.

Keywords: chemotherapy, head and neck cancer, oral mucositis, radiotherapy, supersaturated calcium phosphate

Contact: Dr. Anwesha Mishra, BDS
Department of Public Health Dentistry, Kalinga Institute of Dental Sciences (KIDS), Kalinga
Institute of Industrial Technology (KIIT) Deemed to be University, Bhubaneswar 751024,
Odisha, India.
E-mail: anwesha.mishra28@gmail.com

J Health Sci Med Res
doi: .10.31584/jhsmr.20261438
www.jhsmr.org

© 2026 JHSMR. Hosted by Prince of Songkla University. All rights reserved.
This is an open access article under the CC BY-NC-ND license
(<http://www.jhsmr.org/index.php/jhsmr/about/editorialPolicies#openAccessPolicy>).

Introduction

Head and neck cancers constitute a diverse group of malignancies originating from the mucosal linings and supporting structures of the oral cavity, pharynx, larynx, and adjacent regions, representing a significant global health challenge due to their complex etiologies and varied prognosis¹. The distribution and behaviour of these tumours are influenced by established risk factors such as tobacco and alcohol consumption, while emerging causes include oncogenic viral influences².

The treatment of head and neck cancer generally involves a combination of methods, such as surgery, radiotherapy, chemotherapy, or a mix of chemoradiotherapy, which are chosen based on the tumour's stage, its location, and factors specific to the patient. Radiotherapy, whether used alone or alongside chemotherapy, is a fundamental part of managing locally advanced cases because of its success in controlling the disease locally and organ preservation. However, these treatment options often lead to considerable oral side effects, especially oral mucositis, which can negatively impact both the patient's adherence to the treatment plan and their overall quality of life³⁻⁶.

Oral mucositis is one of the most common and clinically significant adverse effects encountered during cancer therapy of head and neck cancer patients receiving radiotherapy or chemotherapy⁶. Clinically, mucositis manifests as erythema, mucosal atrophy, and painful ulcerations that hinder eating, speaking, and maintaining oral hygiene. This functional impairment reduces patient comfort and well-being while increasing the risk of secondary infections and systemic complications, which can prolong recovery and escalate the need for supportive care⁷. The incidence and severity of oral mucositis in head and neck cancer patients are notably high: reports indicate that a large proportion of patients undergoing combined modality treatment will experience mucositis, with a significant subset

developing severe, ulcerative forms that require nutritional support or hospitalization⁸.

The biological basis of mucositis is explained through a temporal model consisting of sequential phases—initiation, upregulation of signalling pathways, signal amplification, ulceration, and healing⁹. Initiation occurs when ionizing radiation or chemotherapeutic agents cause direct Deoxyribonucleic Acid (DNA) damage and generate reactive oxygen species (ROS), which harm epithelial and submucosal cells¹⁰. The upregulation and amplification phases involve the activation of transcription factors such as NF- κ B and an increased production of pro-inflammatory cytokines, including tumour necrosis factor alpha (TNF- α), interleukin (IL)-1, and IL-6, which amplify tissue injury¹¹. The breakdown of mucosal integrity culminates in the ulcerative phase, characterized by deep, painful lesions¹². The healing phase is marked by epithelial proliferation, differentiation, and remodelling¹³. The clinical consequences of severe oral mucositis are extensive. Beyond pain and dysphagia, patients frequently experience significant reductions in oral intake, leading to weight loss, dehydration, and malnutrition¹⁴. Severe mucositis also increases the likelihood of unplanned hospital admissions, intravenous fluid replacement, and the need for enteral or parenteral nutritional support, thereby escalating healthcare resource use and direct medical costs¹⁵.

A multicentre analysis identified tumour location (e.g., nasopharyngeal or oropharyngeal sites), cumulative radiation doses exceeding thresholds such as 5,000 cGy, and concurrent systemic chemotherapy as major contributors to increased risk and severity¹⁶. On a population level, mucositis translates to both humanistic and economic costs. Patients report substantial decrements in quality of life, with pain, social withdrawal, and functional impairment as key concerns¹⁷.

Economic analyses confirm that radiochemotherapy patients who develop severe mucositis incur markedly higher supportive care costs due to hospitalizations, parenteral nutrition, opioid therapy, and other interventions compared to patients without severe complications¹⁸. Thus, mucositis is not only a clinical challenge but also an economic burden and a target for cost-containment through improved preventive strategies. International guidelines, particularly from the MASCC–Multinational Association of supportive care in cancer, ISOO–International Society of Oral Oncology (MASCC/ISOO) collaboration, provide recommendations on oral hygiene protocols, analgesia, and selected prophylactic measures¹⁹. These guidelines advocate routine mouth care to reduce the risk of infection, topical analgesics and coating agents for symptomatic relief, and the use of preventive approaches with demonstrated clinical benefit²⁰. Yet mucositis remains prevalent in high-risk populations, highlighting the need for additional mechanism-based strategies.

Supersaturated calcium phosphate rinses (SCPR) have emerged as one such option. By replicating the ionic composition of saliva, SCPR supplies bioavailable calcium and phosphate ions to injured mucosa, aiming to restore local ionic balance, support remineralization, and promote wound closure²¹. Supersaturated calcium phosphate rinses have been suggested as a supportive care approach to prevent and manage oral mucositis caused by head and neck cancer treatment. Clinical research on the use of supersaturated calcium phosphate in patients receiving radiotherapy and/or chemotherapy for head and neck cancer has shown mixed results, highlighting the necessity for a thorough assessment of its efficacy^{22–24}.

Clinical studies—including prospective, retrospective studies, and clinical trials—have examined SCPR in head and neck cancer patients, with some reporting reductions in mucositis severity, opioid requirements, and treatment interruptions, while others show more variable results²⁵.

Recent guideline updates further emphasize the importance of consolidating current evidence to guide practice²⁶.

This review, therefore, synthesized the available studies on SCPR in the prevention and management of oral mucositis in patients undergoing radiotherapy and/or chemotherapy for head and neck cancer.

Material and Methods

Study protocol and registration

The study adhered completely to the PRISMA 2020 guidelines, which stand for Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Additionally, it has been officially registered with PROSPERO, the global registry for systematic reviews, and can be accessed at <https://www.crd.york.ac.uk/prospero/> under the registration number CRD42025634616.

Systematic review registration

<https://www.crd.york.ac.uk/prospero/>, under registration ID: CRD42025634616.

Research question

The systematic review addressed the research question: How effective is supersaturated calcium phosphate in treating patients with head and neck cancer ?

Search strategies

A comprehensive and organized search was performed to locate research articles using specific keywords that explore the effects of supersaturated calcium phosphate on individuals with head and neck cancer. No restrictions were applied on the year of publication, and all relevant studies available up to the final search date were considered for inclusion. Table 1 outlines the total number of studies completed in each database. Full-text articles were electronically searched across four databases using Medical Subject Headings (MeSH) keywords. The studies

were examined in PubMed, Scopus, Web of Science, and Embase, with Google Scholar also included as an additional resource. Two analysts conducted an electronic literature search, selecting articles that met the inclusion criteria. The keywords used were supersaturated calcium phosphate, Radiotherapy, and Head and neck cancer. The Boolean operators “OR” and “AND” were used to combine the keywords (Table 1). A polygot search was conducted in Systematic Review (SR) Accelerator using the same search method as in other databases. Rayyan, a tool for conducting systematic reviews, was employed to remove duplicate studies. Furthermore, two authors reviewed the titles and abstracts of the articles. The chosen articles were then meticulously examined by the authors to determine their eligibility according to the study’s inclusion criteria.

Eligibility criteria

The criteria for inclusion were established using the Participants, Intervention, Comparison, Outcomes (PICO) framework as outlined below:

Population

The study population included global head and neck cancer patients undergoing radiotherapy or chemotherapy who developed oral mucositis.

Intervention

Supersaturated calcium phosphate.

Comparison

Management other than supersaturated calcium phosphate.

Outcome

The outcome was assessed based on severity,

duration, and clinical improvement of oral mucositis as reported in the included studies.

This systematic review focused on original research articles that assessed the effectiveness of supersaturated calcium phosphate in treating oral mucositis among patients with head and neck cancer. Only full-text articles written in English were included. Exclusion criteria encompassed studies involving animal research, non-original articles, such as editorials, reviews, or opinion pieces, research on oral mucositis in cancers other than head and neck cancer, and articles without the full text available. A detailed summary of the inclusion and exclusion criteria is described in Table 2.

Data extraction and synthesis

Eligible articles were selected (Table 2), and data extraction was performed manually by an additional author. The primary evaluating author independently assessed the titles and abstracts from the literature search results, with another reviewer overseeing and verifying the process. In cases of disagreement, discussions were held between the two authors as necessary. The study adhered to the PRISMA flowchart for systematic reviews and meta-analyses. A total of 92 studies were identified based on the search criteria. After removing 27 duplicates using Rayyan software, 65 records were screened. Of these, 48 were excluded after reviewing the titles and abstracts. Full-text screening was conducted for 17 studies, but 9 could not be retrieved. Ultimately, 8 articles were screened, and after exclusions, 6 articles were selected for further review. Additionally, 3 articles from Google Scholar were included, resulting in a total of 9 articles in the study (Figure 1). This systematic review collected data on the following parameters: author details, year of publication, journal, study title, study location, study design, sample size, study results, and study conclusion.

Table 1 Search strategy used in different electronic databases

PUBMED	("Calcium Phosphates"[MeSH Terms] OR ("calcium phosphate"[Title/Abstract] OR "tricalcium phosphate"[Title/Abstract] OR "caphosol"[Title/Abstract])) AND ("Head and Neck Neoplasms"[MeSH Terms] OR ("esophageal neoplasms"[Title/Abstract] OR "esophageal squamous cell carcinoma"[Title/Abstract] OR "facial neoplasms"[Title/Abstract] OR "eyelid neoplasms"[Title/Abstract] OR "mouth neoplasms"[Title/Abstract] OR "gingival neoplasms"[Title/Abstract] OR "leukoplakia"[Title/Abstract] OR "lip neoplasms"[Title/Abstract] OR "palatal neoplasms"[Title/Abstract] OR "salivary gland neoplasms"[Title/Abstract] OR "tongue neoplasms"[Title/Abstract] OR "otorhinolaryngologic neoplasms"[Title/Abstract] OR "ear neoplasms"[Title/Abstract] OR "laryngeal neoplasms"[Title/Abstract] OR "nose neoplasms"[Title/Abstract] OR "pharyngeal neoplasms"[Title/Abstract] OR "parathyroid neoplasms"[Title/Abstract] OR "squamous cell carcinoma of head and neck"[Title/Abstract] OR "thyroid neoplasms"[Title/Abstract] OR "thyroid cancer"[Title/Abstract] OR "papillary thyroid nodule"[Title/Abstract] OR "tracheal neoplasms"[Title/Abstract])) AND ("Radiotherapy"[MeSH Terms] OR ("brachytherapy"[Title/Abstract] OR "chemoradiotherapy"[Title/Abstract] OR "pituitary irradiation"[Title/Abstract] OR "craniospinal irradiation"[Title/Abstract] OR "heavy ion radiotherapy"[Title/Abstract] OR "proton therapy"[Title/Abstract] OR "hemibody irradiation"[Title/Abstract] OR "lymphatic irradiation"[Title/Abstract] OR "radioimmunotherapy"[Title/Abstract] OR "radiotherapy dosage"[Title/Abstract] OR "radioisotope teletherapy"[Title/Abstract] OR "whole body irradiation"[Title/Abstract] OR "x ray therapy"[Title/Abstract]))
EMBASE	('Calcium Phosphates'/exp OR ('calcium phosphate':ti,ab OR 'tricalcium phosphate':ti,ab OR 'caphosol':ti,ab)) AND ('Head and Neck Neoplasms'/exp OR ('esophageal neoplasms':ti,ab OR 'esophageal squamous cell carcinoma':ti,ab OR 'facial neoplasms':ti,ab OR 'eyelid neoplasms':ti,ab OR 'mouth neoplasms':ti,ab OR 'gingival neoplasms':ti,ab OR 'leukoplakia':ti,ab OR 'lip neoplasms':ti,ab OR 'palatal neoplasms':ti,ab OR 'salivary gland neoplasms':ti,ab OR 'tongue neoplasms':ti,ab OR 'otorhinolaryngologic neoplasms':ti,ab OR 'ear neoplasms':ti,ab OR 'laryngeal neoplasms':ti,ab OR 'nose neoplasms':ti,ab OR 'pharyngeal neoplasms':ti,ab OR 'parathyroid neoplasms':ti,ab OR 'squamous cell carcinoma of head and neck':ti,ab OR 'thyroid neoplasms':ti,ab OR 'thyroid cancer':ti,ab OR 'papillary thyroid nodule':ti,ab OR 'tracheal neoplasms':ti,ab)) AND (Radiotherapy/exp OR (brachytherapy':ti,ab OR chemoradiotherapy':ti,ab OR 'pituitary irradiation':ti,ab OR 'craniospinal irradiation':ti,ab OR 'heavy ion radiotherapy':ti,ab OR 'proton therapy':ti,ab OR 'hemibody irradiation':ti,ab OR 'lymphatic irradiation':ti,ab OR radioimmunotherapy':ti,ab OR 'radiotherapy dosage':ti,ab OR 'radioisotope teletherapy':ti,ab OR 'whole body irradiation':ti,ab OR 'x ray therapy':ti,ab))
SCOPUS	(INDEXTERMS("Calcium Phosphates") OR (TITLE-ABS("calcium phosphate") OR TITLE-ABS("tricalcium phosphate") OR TITLE-ABS("caphosol"))) AND (INDEXTERMS("Head and Neck Neoplasms") OR (TITLE-ABS("esophageal neoplasms") OR TITLE-ABS("esophageal squamous cell carcinoma") OR TITLE-ABS("facial neoplasms") OR TITLE-ABS("eyelid neoplasms") OR TITLE-ABS("mouth neoplasms") OR TITLE-ABS("gingival neoplasms") OR TITLE-ABS("leukoplakia") OR TITLE-ABS("lip neoplasms") OR TITLE-ABS("palatal neoplasms") OR TITLE-ABS("salivary gland neoplasms") OR TITLE-ABS("tongue neoplasms") OR TITLE-ABS("otorhinolaryngologic neoplasms") OR TITLE-ABS("ear neoplasms") OR TITLE-ABS("laryngeal neoplasms") OR TITLE-ABS("nose neoplasms") OR TITLE-ABS("pharyngeal neoplasms") OR TITLE-ABS("parathyroid neoplasms") OR TITLE-ABS("squamous cell carcinoma of head and neck") OR TITLE-ABS("thyroid neoplasms") OR TITLE-ABS("thyroid cancer") OR TITLE-ABS("papillary thyroid nodule") OR TITLE-ABS("tracheal neoplasms")))) AND (INDEXTERMS(Radiotherapy) OR (TITLE-ABS(brachytherapy*) OR TITLE-ABS(chemoradiotherapy*) OR TITLE-ABS("pituitary irradiation") OR TITLE-ABS("craniospinal irradiation") OR TITLE-ABS("heavy ion radiotherapy") OR TITLE-ABS("proton therapy") OR TITLE-ABS("hemibody irradiation") OR TITLE-ABS("lymphatic irradiation") OR TITLE-ABS(radioimmunotherapy*) OR TITLE-ABS("radiotherapy dosage") OR TITLE-ABS("radioisotope teletherapy") OR TITLE-ABS("whole body irradiation") OR TITLE-ABS("x ray therapy")))
WEB OF SCIENCE	ALL=((calcium phosphate OR tricalcium phosphate OR caphosol)) AND (((((((((ALL=(Head and Neck Neoplasms) OR ALL=(esophageal neoplasms) OR ALL=(esophageal squamous cell carcinoma) OR ALL=(facial neoplasms) OR ALL=(eyelid neoplasms) OR ALL=(mouth neoplasms) OR ALL=(gingival neoplasms) OR ALL=(leukoplakia) OR ALL=(lip neoplasms) OR ALL=(palatal neoplasms) OR ALL=(salivary gland neoplasms) OR ALL=(tongue neoplasms) OR ALL=(otorhinolaryngologic neoplasms) OR ALL=(ear neoplasms) OR ALL=(laryngeal neoplasms) OR ALL=(nose neoplasms) OR ALL=(pharyngeal neoplasms) OR ALL=(parathyroid neoplasms) OR ALL=(squamous cell carcinoma of head and neck) OR ALL=(thyroid neoplasms) OR ALL=(thyroid cancer) OR ALL=(papillary thyroid nodule) OR ALL=(tracheal neoplasms) AND (((((((((ALL=(Radiotherapy) OR ALL=(brachytherapy) OR ALL=(chemoradiotherapy) OR ALL=(pituitary irradiation) OR ALL=(craniospinal irradiation) OR ALL=(heavy ion radiotherapy) OR ALL=(proton therapy) OR ALL=(hemibody irradiation) OR ALL=(lymphatic irradiation) OR ALL=(radioimmunotherapy) OR ALL=(radiotherapy dosage) OR ALL=(radioisotope teletherapy) OR ALL=(whole body irradiation) OR ALL=(x ray therapy)

Risk of bias assessment

The quality of all the studies was assessed using the National Institutes of Health (NIH) tool, developed by the National Heart, Lung, and Blood Institute (NHLBI). This evaluation adhered to the criteria specified in the checklists for reporting both observational and controlled intervention studies. Green circles signify “yes,” red circles denote “no,” while yellow, grey, and blue circles represent “not reported,” “cannot determine,” and “not applicable,” respectively. Two reviewers evaluated the risk of bias in the included articles to determine the quality of the studies. If disagreements arose, a third reviewer was consulted (Table 3).

Results

Study selection results

A total of 92 studies were identified based on the search criteria. After removing 27 duplicates, 65 records were screened. Of these, 48 were excluded after reviewing the Title and Abstract. Full-text screening was conducted for 17 studies, but 9 could not be retrieved. Ultimately, 8 articles were screened, and after exclusions, 6 articles were chosen for further review. Additionally, 3 articles from Google Scholar were included, bringing the total to 9 articles in the study (Figure 1).

Data summary of the included studies

This systematic review gathered information on several parameters, including the author’s details, the year and journal of publication, the study’s title, location, design, sample size, findings, and conclusions (Table 4). The review examined data across various key parameters, focusing on different study types. Most of the studies were clinical trials. Among the nine studies included in this systematic review, three were conducted in the United States, two in Europe (specifically the Netherlands and Belgium), one in the United Kingdom, one in Poland, one in Canada, and one multi-center study involved institutions across multiple countries. This distribution suggests that the majority of the available evidence is derived from Western populations. Among the studies included in the review, five found a positive impact on reducing oral mucositis with the use of supersaturated calcium phosphate, while four studies reported no significant effect on mucositis from its use.

Outcome measures

The efficacy of supersaturated calcium phosphate was evaluated based on the outcome measures reported in the included studies. These outcomes included statistically significant differences in the severity, duration, or symptom

Table 2 Inclusion and exclusion table

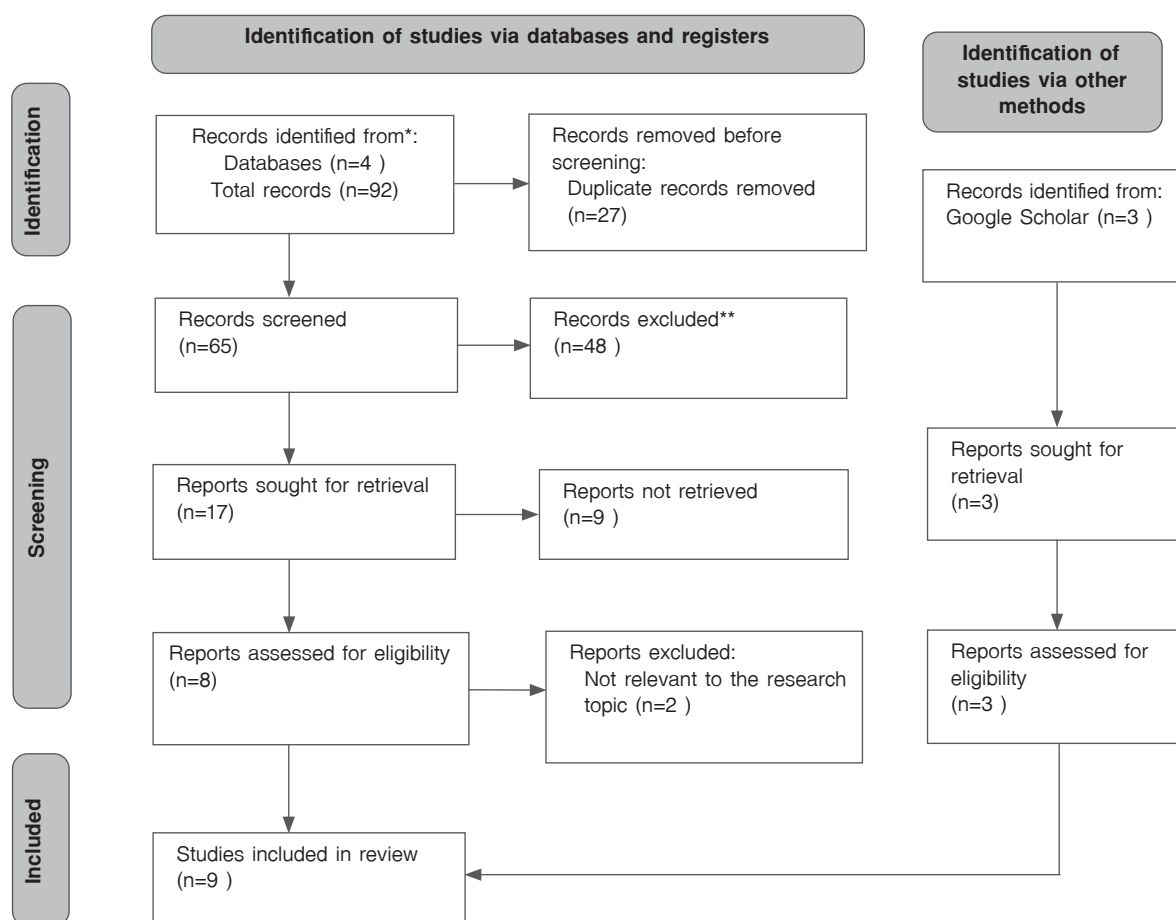
Inclusion criteria	Exclusion criteria
Articles that are related to Oral Mucositis induced by Head and Neck Cancer.	Studies examining the impact of SCPR on OM alongside other carcinoma or cancer treatments
Articles that are related to the use of supersaturated calcium phosphate to treat Oral Mucositis in Head and Neck Cancer Patients.	Animal studies, Editorials, and reviews were excluded.
Articles that are available in full texts and are in English	Research articles written in languages other than english.

SCPR=supersaturated calcium phosphate, OM=oral mucositis

Table 3 Risk of bias assessment according to NIH tool

Stokman, et al.	Curtis T, et al.	Lambrecht, et al.	Wayne Taylor	Rao, Nikhi G, et al.	Stringer J, et al.	Wong, Kee H, et al.	Kiprian Dorota	Justin Brock
Good	Fair	Good	Fair	Good	Good	Fair	Fair	Good

Risk of bias was assessed using the National Institutes of Health (NIH) Quality Assessment Tool. Studies highlighted in green indicate good methodological quality (low risk of bias), yellow indicates fair or moderate methodological quality (moderate risk of bias), and red indicates poor methodological quality (high risk of bias). NIH=National Institute of Health



*Total studies included=9, (6 Studies from the databases + 3 studies from google scholar)

Figure 1 Flow chart representing the search of articles in this systematic review

scores of oral mucositis, as well as reported clinical improvements such as reduced severity of oral mucositis, decreased need for opioid analgesics, enhanced oral comfort, and fewer treatment interruptions. Due to the heterogeneity in study design, outcome measures, and reporting formats, effect size metrics such as odds ratios or relative risks were not consistently available across studies. The majority of studies demonstrated that this compound

effectively mitigates oral mucositis, a frequent side effect of radiation therapy for head and neck cancer. Among the studies examined, five confirmed the effectiveness of supersaturated calcium phosphate, while one study also highlighted that involving a Health Advisor for head and neck cancer patients enhanced outcomes. However, four articles did not report favourable results in treating oral mucositis.

Table 4 Vital features of some of the studies included in this systematic review

Study Reference	Details of the author	Year of publication & Journal	Title of the study	Place of study	Study design	Sample size	Results	Conclusion
[15]	MA Stokman FR Burlage FKL Spijkervet	2012 International journal of Dental Hygiene	The effect of a calcium phosphate mouth rinse on (chemo) radiation induced oral mucositis in head and neck cancer patients: A prospective study.	University Medical Center Groningen, Netherlands.	Clinical trials	39	There were no subjective outcomes on MTS concerning the development and severity of mucositis between the CP group and the control group. The OM data for the two groups yielded a p-value of 0.0002 in the student's t-test, indicating a statistically significant improvement with SCPR treatment.	To sum up, the CP mouth rinse does not affect the occurrence, length, or intensity of oral mucositis in patients undergoing chemo radiation for head and neck cancer. In summary, despite the small sample size of 42 patients, the caphosol-treated group demonstrated a statistically significant decrease in the incidence of OM.
[16]	Curtis T. Miyamoto, Jessica Wobb, Bizhan Mically, Shidong Li, Mohan P. Achary	2012 Journal of Cancer Therapy	A Retrospective Match Controlled Study of Supersaturated Calcium Phosphate Oral Rinse vs Supportive Care for Radiation Induced Oral Mucositis	Temple University Hospital, Department of Radiation Oncology, Philadelphia, USA	Clinical trials	21	The randomized clinical trials indicate that using a supersaturated calcium phosphate mouthrinse for patients undergoing chemotherapy for head and neck cancer does not significantly decrease the frequency, duration, or severity of oral mucositis.	
[17]	Maarten Lambrecht, Carole Mercier, Yasmyne Geussens, Sandra Nuyts	2013 Support care cancer	The effect of a supersaturated calcium phosphate mouth rinse on the development of oral mucositis in head and neck cancer patients treated with chemo radiation	Radiotherapy Department of the university Hospital of Leuven, Belgium	Randomized clinical trial	60		

Table 4 (continued)

Study Reference	Details of the author	Year of publication & Journal	Title of the study	Place of study	Study design	Sample size	Results	Conclusion
[18]	D.Wayne Taylor	2013 Clinical Medicine and Diagnostics	A Business Impact study of the use of a supersaturated calcium phosphate oral rinse (SCPOR) in the prevention and treatment of oral mucositis	Canadian Hospitals and cancer centres.	Cohort Study	4550	With 4,550 instances of head and neck cancers, the national net savings would be at least \$3,016,650.	Implementing SCPOR for the treatment of OM would result in a total national savings for both BMT and head and neck cancer.
[19]	Nikhil G Rao, Andy Trotti, Jongphil kim, Michael J schell, Xiuhua zhao, Robert j andur, David m brizel, Mark s chambers, Jimmy j caudell, Curtis miyamoto, David I Rosenthal	2014 Journal of oral oncology	Phase II multicenter trial of caphosol for the reduction of mucositis in patients receiving radiation therapy for head and neck cancer	Moffitt Cancer Center (MCC), MD Anderson Cancer Center (MDACC), Duke University Cancer Center (DUCC), University of Florida (UF) and Temple University Cancer Center (TUCC)	Phase II multicenter trial	98	The trial failed to reject the null hypothesis, as all evaluable patients had mucositis of WHO grade > or equal to 2.	In summary, despite patients reporting slight symptom relief, our investigation did not reveal any additional harm from caphosol use.
[21]	J.Stringer,R. knowles,C.Finchett,P. Mackereth,J.Mannan, N.Slevin	2015 Journal of Radiotherapy Practice.	Health advisor facilitated mouth care regime for patients with head and neck cancers undergoing intensity-modulated radiotherapy.	The Christie NHS Foundation Trust, Withington, Manchester ,UK.	Randomized clinical trial	216	100% compliance with necessary exams, referrals, and treatment adherence was made possible by the Health Advisor's presence.	Establishing a HA position in radiation departments is advised in order to support lifestyle evaluations, referrals, and adherence to constructive behavioral modifications.

Table 4 (continued)

Study Reference	Details of the author	Year of publication & Journal	Title of the study	Place of study	Study design	Sample size	Results	Conclusion
[22]	Kee H Wong, Aleksandra Kuciejewska, Mansour T.A Sharabiani, Brian Ng Cheng Hin, Sonja Hoy, Tara Hurley, Joanna Rydon, Lorna Grove, Ana Santos, Motoko Ryugenji, Shreerang a bhide, Chris m nutting, Kevin j Harrington, Kate L Newbold.	2016 The journal of Radiotherapy and oncology	A randomized controlled trial of caphosol mouthwash in management of radiation induced mucositis in head and neck cancer.	Royal Marsden Hospital	Phase III non blinded randomised controlled trial	215	Between the intervention and control groups, there was no difference in the incidence of severe OM.	In head and neck malignancies, caphosol had no effect on the frequency or length of severe OM during or after radiation therapy.
[23]	Dorota kiprian, Andrzej jarzabski, Andrzej Kawecki	2016 Journal of contemporary oncology	Evaluation of efficacy of caphosol in prevention and alleviation of acute side effects in patients treated with radiotherapy for head and neck cancers.	Comprehensive cancer Center, Warsaw, Poland.	Randomized clinical trial	100	The experimental group of patients in the CTV area and the boost volume area showed a significant decrease in the severity of irradiation-induced mucositis as compared to the control group.	Caphosol improves oral cavity comfort in patients receiving radiation therapy for head and neck cancers by lessening the severity of acute mucositis, dysphagia, and xerostomia.
[24]	Justin Brock, Chris Morris, Kathleen Hotze, Brian Pikkula	2018 Journal of cancer therapy	Supersaturated Calcium Phosphate Rinse vs. Standard of Care for Mitigating Mucositis in Head and Neck Chemoradiation	USA	Clinical Trials	20	There was a statistically significant (p-value>0.001) decrease in peak OM and a delay in OM start that was not statistically significant in the SSCPR group	This retrospective analysis shows that using powdered SSCPR to mitigate oral mucositis is a safe and efficient approach.

Discussion

Radiation-induced mucositis is a frequent and often serious complication of radiation therapy for cancers of the head and neck. This condition arises when radiation harms the epithelial cells that line the oral and gastrointestinal mucosa, resulting in inflammation, ulceration, and pain. Typically, mucositis begins to manifest within 2–3 weeks of initiating radiation treatment and may continue for several weeks after the therapy concludes. Symptoms include redness, swelling, and painful sores in the mouth and throat, which can greatly affect a patient's ability to eat, drink, and speak.

The severity of mucositis can vary from mild discomfort to intense pain that necessitates opioid pain relief and may even cause interruptions in treatment. Management approaches involve maintaining proper oral hygiene, applying topical pain relievers, and providing nutritional support. Among the many products available for treating oral mucositis, Caphosol is a notable option. This product is a supersaturated calcium phosphate solution specifically formulated to moisturize and lubricate the oral mucosa. It helps restore vital minerals such as calcium phosphate, which are crucial for repairing and maintaining the mucosal lining's integrity.

This systematic review focused on evaluating the effectiveness of supersaturated calcium phosphate in managing radiation-induced oral mucositis among patients with head and neck cancer. This is the inaugural systematic review to assess the efficacy of supersaturated calcium phosphate in treating radiation-induced oral mucositis among patients with head and neck cancer. Based on the analysis of the included nine studies, our results reveal a significant impact on oral mucositis when using supersaturated calcium phosphate.

Out of these studies, five reported a considerable decrease in oral mucositis with the application of this compound. In contrast, four studies did not find

supersaturated calcium phosphate to be effective. Research conducted at the University Medical Center Groningen in the Netherlands revealed that while the Calcium Phosphate mouth rinse significantly alleviates oral pain in head and neck cancer patients, it does not lead to a notable decrease in the occurrence, duration, or severity of oral mucositis in those undergoing chemoradiation for head and neck cancer¹⁵.

Lambrecht et al. also support the results from the Netherlands, determining that incorporating the CP mouth rinse did not enhance the frequency, duration, or severity of oral mucositis or other acute toxicities related to treatment in head and neck cancer patients undergoing (chemo) radiation. Consequently, there is no current evidence to justify its routine use in clinical settings¹⁷.

A randomized controlled trial carried out in the United States of America (USA) lends further support to the research by Lambrecht et al. and studies from the Netherlands. Although the trial did not show a significant decrease in the occurrence of mucositis with the use of Caphosol, it offered valuable insights into patient experiences, highlighting the effectiveness of structured data collection methods in clinical trials¹⁹.

According to the study by Wong et al., the use of Caphosol mouthwash did not lead to a significant decrease in the occurrence or length of severe oral mucositis in patients undergoing radiotherapy for head and neck cancer. These results indicate that other approaches might be necessary to effectively address mucositis caused by radiation²². A study at Temple University Hospital reveals that a supersaturated calcium phosphate oral rinse is effective in treating mucositis in patients receiving Intensity Modulated Radiation Therapy (IMRT), while also reducing their need for hospitalization. The research showed that only 33% of patients using Caphosol required PEG tube placement, compared to 57% in the group receiving standard supportive care, indicating that Caphosol may

better support oral intake. Additionally, none of the patients in the Caphosol group were hospitalized due to mucositis, whereas 19% of the control group needed hospitalization, suggesting Caphosol's potential in minimizing severe complications.

Overall, the findings suggest that Caphosol is an effective treatment for managing oral mucositis in patients undergoing radiation therapy, with added benefits of reducing hospitalization and related costs¹⁶. An observational study conducted in Canadian hospitals suggests that Super saturated calcium phosphate (SCPOR) could result in savings of between 3,085 and 6,085 per patient, with a potential return on investment ranging from 464.9% to 915.0%. The economic impact of OM includes extra treatment expenses such as pain management, intravenous hydration, and extended hospital stays, all of which SCPOR effectively reduced¹⁸. Furthermore, research underscores that the involvement of a Health Advisor [HA] results in favourable behavioural changes among patients undergoing IMRT for head and neck cancer²¹. A Polish study also corroborates the positive impact of Caphosol²³. Additionally, a retrospective study from the United States suggests that supersaturated calcium phosphate is a safe and effective treatment for oral mucositis²⁴.

Limitations

This systematic review has certain limitations, such as studies published in the English language were included, which may have resulted in the exclusion of relevant research published in other languages. The search strategy did not encompass all databases. Additionally, heterogeneity in study designs, sample sizes, and outcome assessment methods limited direct comparison across studies and meta-analysis. Furthermore, there are no recent clinical trials that highlight the beneficial effects of supersaturated calcium phosphate on radiation-induced oral mucositis.

Conclusion

Studies consistently show that supersaturated calcium phosphate is effective in reducing the occurrence, duration, and severity of oral mucositis in patients with head and neck cancer. Additionally, comprehensive clinical trials are necessary to determine the precise effects of Caphosol on oral mucositis.

Acknowledgement

We would like to acknowledge the entire Department of Public Health Dentistry, Kalinga Institute of Dental Sciences (KIDS), Kalinga Institute of Industrial Technology (KIIT) Deemed to be University, for their support.

Funding sources

There is no source of funding recieved.

Conflict of interest

There is no conflict of interest.

References

1. Trotti A, Bellm LA, Epstein JB, Frame D, Fuchs HJ, Gwede CK, et al. Mucositis incidence, severity and associated outcomes in patients with head and neck cancer receiving radiotherapy with or without chemotherapy: a systematic literature review. *Radiother Oncol* 2003;66:253–62.
2. Sonis ST, Elting LS, Keefe D, Peterson DE, Schubert M, Hauer-Jensen M, et al. Perspectives on cancer therapy-induced mucosal injury: pathogenesis, measurement, epidemiology, and consequences for patients. *Cancer* 2004;100:1995–2025.
3. Rubenstein EB, Peterson DE, Schubert M, Keefe D, McGuire D, Epstein J, et al. Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. *Cancer* 2004;100:2026–46.
4. Sonis ST. The pathobiology of mucositis. *Nat Rev Cancer* 2004;4:277–84.
5. Tromp DM, Brouha XD, de Leeuw JR, Hordijk GJ, Winnubst JA. Psychological factors and patient delay in patients with head and neck cancer. *Eur J Cancer* 2004;40:1509–16.

6. Stokman MA, Sonis ST, Dijkstra PU, Burgerhof JG, Spijkervet FK. Assessment of oral mucositis in clinical trials: impact of training on evaluators in a multi-centre trial. *Eur J Cancer* 2005;41:1735–8.
7. Vera-Llonch M, Oster G, Hagiwara M, Sonis S. Oral mucositis in patients undergoing radiation treatment for head and neck carcinoma: risk factors and clinical consequences. *Cancer* 2006;106:329–36.
8. Keefe DM, Schubert MM, Elting LS, Sonis ST, Epstein JB, Raber-Durlacher JE, et al. Updated clinical practice guidelines for the prevention and treatment of mucositis. *Cancer* 2007;109:820–31.
9. Elting LS, Cooksley CD, Chambers MS, Garden AS. Risk, outcomes, and costs of radiation-induced oral mucositis among patients with head-and-neck malignancies. *Int J Radiat Oncol Biol Phys* 2007;68:1110–20.
10. Russo G, Haddad R, Posner M, Machtay M. Radiation treatment breaks and ulcerative mucositis in head and neck cancer. *Oncologist* 2008;13:886–98.
11. Nonzee NJ, Dandade NA, Markossian T, Agulnik M, Argiris A, Patel JD, et al. Evaluating the supportive care costs of severe radiochemotherapy-induced mucositis and pharyngitis: results from a Northwestern University cost-of-cancer program pilot study. *Cancer* 2008;113:1446–52.
12. Haas ML, Treister NS, Manyak MJ. Reduction of painful oral mucositis by supersaturated calcium phosphate oral rinse in head and neck cancer patients receiving chemotherapy and radiation. *Int J Radiat Oncol Biol Phys* 2008;72(1 Suppl):S406.
13. Rosenthal DI, Trotti A. Strategies for managing radiation-induced mucositis in head and neck cancer. *Semin Radiat Oncol* 2009;19:29–34.
14. Peterson DE, Bensadoun RJ, Roila F. Management of oral and gastrointestinal mucositis: ESMO clinical recommendations. *Ann Oncol* 2009;20(Suppl 4):iv174–7.
15. Stokman MA, Burlage FR, Spijkervet FK. The effect of a calcium phosphate mouth rinse on (chemo) radiation induced oral mucositis in head and neck cancer patients: a prospective study. *Int J Dent Hyg* 2012;10:175–80.
16. Miyamoto CT, Wobb J, Micaily B, Li S, Achary MP. A retrospective match controlled study of supersaturated calcium phosphate oral rinse vs. supportive care for radiation induced oral mucositis. [Journal not provided].
17. Lambrecht M, Mercier C, Geussens Y, Nuyts S. The effect of a supersaturated calcium phosphate mouth rinse on the development of oral mucositis in head and neck cancer patients: a single-center, randomized, prospective study. *Support Care Cancer* 2013;21:2663–70.
18. Taylor DW. A business impact study of the use of a supersaturated calcium phosphate oral rinse (SCPOR) in the prevention and treatment of oral mucositis. *Clin Med Diagn* 2013;3:82–7.
19. Rao NG, Trotti A, Kim J, Schell MJ, Zhao X, Amdur RJ, et al. Phase II multicenter trial of Caphosol for the reduction of mucositis in patients receiving radiation therapy for head and neck cancer. *Oral Oncol* 2014;50:765–9.
20. AfzaliNasab S, Mehr MT, Khajehahmadi S, Bagherpour A. Maxillary sinus squamous cell carcinoma during pregnancy: a new case report. *Cumhuriyet Dent J* 2015;18:364–9.
21. Stringer J, Knowles R, Finchett C, Mackereth P, Mannan J, Slevin N. Health advisor facilitated mouth care regime for patients with head and neck cancers undergoing intensity-modulated radiotherapy. *J Radiother Pract* 2015;14:353–61.
22. Wong KH, Kuciejewska A, Sharabiani MT, Ng-Cheng-Hin B, Hoy S, Hurley T, et al. A randomised controlled trial of Caphosol mouthwash in management of radiation-induced mucositis in head and neck cancer. *Radiother Oncol* 2017;122:207–11.
23. Kiprian D, Jarzabski A, Kaweck A. Evaluation of efficacy of Caphosol in prevention and alleviation of acute side effects in patients treated with radiotherapy for head and neck cancers. *Contemp Oncol (Pozn)* 2016;20:389–93.
24. Brock J, Morris C, Hotze K, Pikkula B. Supersaturated calcium phosphate rinse vs. standard of care for mitigating mucositis in head and neck chemoradiation. *J Cancer Ther* 2018;9:262–7.
25. Buch S, Babu S, Rao S. Indiscriminate use of smokeless tobacco leading to oral cancer at a young age: a case report with literature review on tobacco consumption. *Cumhuriyet Dent J* 2019;22:477–80.
26. Elad S, Cheng KK, Lalla RV, Yarom N, Hong C, Logan RM, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. *Cancer* 2020;126:4423–31.