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SYSTEMATIC REVIEW: THE USE OF PROPOLIS MOUTHWASH IN REDUCING MUCOSITIS IN CANCER PATIENTS UNDERGOING CHEMOTHERAPY AND RADIATION THERAPY

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ABSTRACT
A systematic review of randomized clinical trials in cancer patients on the effectiveness of propolis mouthwash use in post-chemo and radiation cancer patients. Oral mucositis (OM) is a common and highly symptomatic complication of cancer therapy that affects function, quality of life. Chemotherapy and radiation are the most widely used interventions in cancer treatment. The prevalence of oral mucositis side effects among HNC patients is 93.9%. Research on the management of OM is still ongoing. This study aims to analyze a systematic review of the use of propolis in preventing and reducing the severity of oral mucositis in cancer patients undergoing chemo- and radiation therapy. Four databases through article searches tailored to the formulation of PICO questions consisting of ScienceDirect, Pubmed, ProQuest, Sage journals and EBSCO, A total of 2,252 articles were identified, and 8 articles were included in the final analysis. Of the ten articles selected, there were 6 articles that were suitable for oral mucositis treatment interventions that showed the effectiveness of using propolis mouthwash to treat ral mucositis with a Randomized Controlled Trial (RCT) design. The use of propolis mouthwash for oral mucositis can be done to overcome and prevent oral mucositis in cancer patients undergoing chemo and radiation therapy.

Keywords: cancer; chemotherapy; mucositis; propolis; radiation

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INTRODUCTION

Cancer is a disease that can affect a person's physical and psychological condition from the time of diagnosis, through therapy, and after becoming a cancer survivor. Cancer is characterized by uncontrolled cell growth (proliferation) and spreading to other parts of the body (Brown et al., 2023). Uncontrolled proliferation refers to the rapid increase in cell number. According to data from the World Health Organization (WHO, 2020), cancer ranks as the leading cause of death worldwide. Based on GLOBOCAN 2020 data, the incidence and mortality of cancer worldwide are estimated at 19.3 million new cases and 10 million deaths due to cancer (Sung et al., 2021).Various treatment modalities for cancer include surgery, chemotherapy, and radiation. Chemotherapy and radiation are the most commonly used interventions in cancer treatment. Although these treatments can improve patients' quality of life, they have several side effects. The side effects include mucositis, xerostomia (dry mouth), bacterial, fungal, and viral infections (especially in neutropenic patients), dental caries, and loss of taste sensation (Naidu et al., 2004). The term oral mucositis emerged in the 1980s to describe inflammation of the oral mucosa caused by chemotherapy and radiation. Oral mucositis worsens the patient's condition, leading to morbidity and mortality.

The prevalence of oral mucositis side effects among 294 head and neck cancer (HNC) patients was 93.9%. The most common was oral mucositis at 97.3%, followed by

xerostomia at 84.4%, while 64.6% experienced dysphagia, 53.7% reported altered taste sensation, and 19% had oral fungal infections, with an average pain score of 4 (Mohammed et al., 2024). Cancer patients undergoing chemotherapy experience mucositis side effects in approximately 30-40% of cases, and nearly 90% of head and neck cancer patients receiving chemotherapy and radiation. The development of mucositis depends not only on the anticancer regimen, dosage, and number of cycles but also on patient characteristics.The type of chemotherapy drugs used determines the severity of oral mucositis. Some drugs affecting mucositis include 5-FU (fluorouracil) and combinations with Irinotecan (Xeliri combination) and the combination of irinotecan and oxaliplatin (FOLFOX). Early stages of these drugs cause diarrhea due to increased acetylcholine resulting from increased saliva production, increased mucus-producing cells, and damage to gastrointestinal tract cell structures. Cisplatin can cause mucositis by inhibiting saliva production and damaging the small intestine (ileum). The severity of gastrointestinal lesions with cisplatin administration is higher than other drugs like oxaliplatin and carboplatin (Pulito et al., 2020). Anti-cancer regimens including 5-Fluorouracil (5-FU), cisplatin, FOLFOX, and dihydropyrimidine dehydrogenase deficiency (an important enzyme in 5-FU catabolism) are relevant factors (Pulito et al., 2020).

Oral mucositis is inflammation of the mucosa characterized by color changes, atrophy, ulceration, edema, and local perfusion changes (Naidu et al., 2004). This condition is marked by inflammation and ulceration of the oral mucosa, causing pain, difficulty swallowing, and impacting the patient's quality of life. The impact of oral mucositis is associated with pain, odynophagia, dehydration, and malnutrition. Symptoms such as pain and discomfort can lead to patients being unable to tolerate chemotherapy or radiation, resulting in toxicity and limiting doses, which affect treatment. Mucositis affects the entire gastrointestinal tract and oral cavity, causing pain, inability to eat, weight loss, and local infection. Patients with severe mucositis often need to reduce chemotherapy regimens, leading to poorer prognosis.Assessment criteria and parameters for mucositis vary. The World Health Organization (WHO) oral mucositis (OM) evaluation considers objective criteria such as the presence of erythema and ulceration, reflecting functional criteria based on the patient’s ability to eat. The Oral Mucositis Assessment Scale (OMAS) quantitatively assesses the ulceration dimension. The Eastern Cooperative Oncology Group (ECOG) mucositis scale assesses general mucositis severity based on anatomical progression, while the National Cancer Institute (NCI) grades mucositis severity based on anatomical location and type of treatment, whether chemotherapy or radiation (Patil et al., 2024; Elad et al., 2020).

Mucositis development consists of several stages: initiation, ulceration, erythema, and hemorrhagic ulceration. Systemic chemotherapy and radiation induce tissue damage causing reactive oxygen species (ROS) release, DNA damage, and death of basal and suprabasal epithelial cells. Risk factors for oral mucositis include age, nutritional status, cancer type, oral care during treatment, and neutrophil count before treatment. Managing mucositis is essential to improve cancer patients’ quality of life and involves multidisciplinary management, mucositis assessment tools, oral hygiene care, pain management, and nutritional support (Zhang et al., 2024).The morbidity and impact of oral mucositis on quality of life are very high. However, there is no effective evidence regarding prophylactic agents or treatments for oral mucositis (Sarvizadeh et al., 2015). Various oral care solutions have been applied to manage mucositis during chemotherapy and radiation, but conflicting side effects are still often experienced by patients undergoing treatment. Management of mucositis has involved several agents, including

anti-inflammatory drugs such as allopurinol and selenium, antimicrobial agents like chlorhexidine, mouthwashes containing chitosan, and natural products such as royal jelly, honey, and curcumin, which have been tested in previous studies for mucositis management (Sorensen et al., 2008; Erdem, 2014; Samira Nezhad et al., 2023; Melani, 2018; Vahid, 2023).

Recent controlled trials found that mouthwash containing propolis is effective in healing wounds or ulcers in the oral cavity (Dodwad et al., 2011). This aligns with research by Dastan et al. (2020) on the use of propolis mouthwash in cancer patients undergoing radiotherapy. Results showed no difference between the propolis and placebo groups in the first week, but significant differences appeared in the second and third weeks. Dysphagia was reported as mild only in the propolis group by the fourth week. Propolis mouthwash is an effective and safe treatment for oral mucositis and dysphagia in patients undergoing head and neck radiotherapy. Propolis contains proteins, amino acids, vitamins, minerals, and flavonoids. As a natural anti-inflammatory product, it inhibits prostaglandin synthesis, activates the thymus gland, enhances the immune system by increasing phagocytosis activity, stimulates cellular immunity, and promotes healing effects on epithelial tissue. Additionally, propolis contains iron and zinc, important for collagen synthesis (Dastan et al., 2020).

Propolis can modulate inflammatory responses. It is a resinous substance collected by honeybees from various plant sources and is rich in bioactive compounds such as flavonoids, phenolic acids, and terpenoids. Propolis is used in homeopathy and herbal practices as an antiseptic, anti-inflammatory, antimycotic, and bacteriostatic agent. When used prophylactically, it has higher effectiveness. Research shows that propolis and flavonoids reduce primary DNA damage in white blood cells. This aligns with Bolouri et al. (2015), who showed that water-based propolis mouthwash is safe and effective for the prevention and treatment of radiotherapy-induced mucositis.Studies have demonstrated that propolis extract has antioxidant and anti-inflammatory effects by inhibiting the production of pro-inflammatory cytokines such as IL-1β, IL-6, and tumor necrosis factor (TNF-α), while increasing the secretion of anti-inflammatory cytokines. The multifaceted nature of propolis's bioactive components contributes to its potential to reduce inflammation and support tissue repair. Moreover, propolis's wound healing properties help prevent and treat mucosal injuries like mucositis caused by chemoradiation.Despite growing knowledge about propolis in managing oral mucositis, there is still insufficient understanding of its mechanisms in mucositis management. Therefore, further research is needed to examine the effects of propolis mouthwash on oral mucositis in patients undergoing chemotherapy and radiation. This research aims to compare ulceration, erythema, and the ability to eat and drink.

METHOD

Design

This study employed a systematic review method by formulating clinical questions based on the PICO framework (Population, Intervention, Comparison Group, and Outcome).

Search Strategy

The search strategy involved several online databases including ScienceDirect, EBSCO, ProQuest, and PubMed. The search terms used were: (Propolis) AND ("oral mucositis" OR stomatitis OR oromucositis OR oral mucositis) AND ("cancer"), management AND (mucositis OR oral mucositis OR mucosal inflammation OR stomatitis) AND cancer treatment.

Eligibility Criteria

Inclusion criteria consisted of articles published within the last five years (2015–2024), including abstracts and full texts; article types: review articles and research articles; study designs: randomized controlled trials (RCTs) and case reports; document type: articles; language: English; keyword relevance; source type: journals; and subject areas focused on Evidence-Based Healthcare and Health & Medical Collections with related keywords. Articles were required to be sourced from journals focused on Evidence-Based Healthcare and Health & Medical Collections. Exclusion criteria included literature reviews, scoping reviews, systematic reviews, umbrella reviews; articles published as book chapters or conference abstracts; and subjects covering materials science, chemistry, immunology and microbiology, neuroscience, environmental science, pharmacology, toxicology, and pharmaceutical sciences. The article selection process was analyzed using a PRISMA diagram, which is presented below.

Selection Process

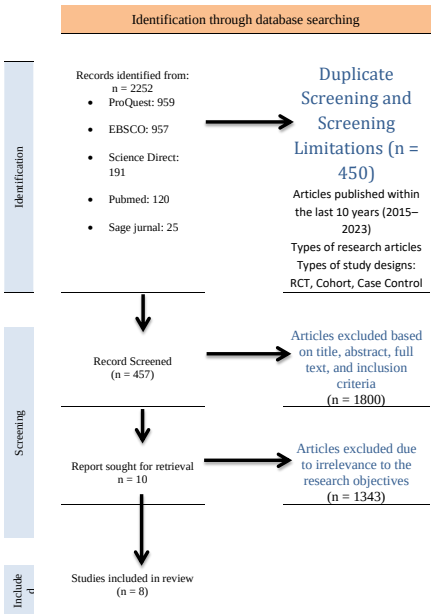
The selection process was based on articles meeting the inclusion criteria: randomized controlled trials involving adult participants aged 18 years and older. The intervention included the use of propolis-based mouthwash with no restrictions on concentration.

Data Collection and Selection

Data collection resulted in eight articles selected for inclusion. Of these, seven articles used a randomized controlled trial (RCT) design, and one article employed an experimental design involving patients on ventilators in the ICU. All selected studies described randomization procedures and used blinding. Most studies aimed to evaluate the effectiveness of propolis mouthwash in managing oral mucositis in patients undergoing chemotherapy and radiotherapy.

Synthesis Methods

Extracted data were synthesized and analyzed based on the PICO-based clinical questions.



Article Selection

An initial identification was conducted across 4 databases, yielding 2,252 articles. Then, duplicate screening based on inclusion/exclusion criteria resulted in 457 articles. Articles

excluded based on title, abstract, full text, and inclusion criteria left 30 articles. Subsequently, 10 articles were excluded due to irrelevance to the study objectives, resulting in 10 articles meeting the eligibility criteria. The final result included 7 articles with randomized controlled trials (RCT) and 1 experimental study. The total number of articles that met the criteria was 6. All articles explained the randomization process and used blinding.

Characteristics of Selected Articles

In general, the characteristics of the studies are presented in Table 1. Six randomized controlled trials (RCTs) meeting the criteria for critical analysis used the Joanna Briggs Institute (JBI) instrument, which is appropriate for RCTs. Most of the research results revealed that the purpose of this study was to evaluate the effectiveness of using mouthwash to manage oral mucositis in patients undergoing chemotherapy and radiotherapy, as described in the table below.

RESULT

Table 1.
Article Analysis

Database	Author, Country, Year	Article Title	Objective	Design	Samples & Measurements	Intervention	Results
ScienceDirect	Akhavan-Karbassi et al., Iran, 2020	*Randomized Double-Blind Placebo-Controlled Trial of Propolis for Oral Mucositis in Patients Receiving Chemotherapy for Head and Neck Cancer*	Assessing the effectiveness and safety of propolis as a mouthwash for chemotherapy-induced mucositis.	RCT	40 patients, WHO scale mucositis measurement.	Propolis 30% vs placebo. Dose 5 ml, 3x/day for 7 days.	Significant reduction in OM & erythema. 65% completely healed by day 7. No significant side effects.
PubMed	Javadzadeh Bolouri et al., Iran, 2015	*Preventing and Therapeutic Effect of Propolis in Radiotherapy Induced Mucositis*	Assessing the effectiveness of propolis for the prevention of radiotherapy-induced mucositis.	Triple-blind RCT	20 patients, mucositis was measured weekly with NCI-CTC.	Propolis 3% or placebo, 15 ml, swallowed, 3x/day for 5 weeks.	Mucositis scores were lower in the propolis group. 8 patients did not experience mucositis.
ScienceDirect	Dastan et al., Iran, 2021	*Efficacy and Safety of Propolis Mouthwash in Radiotherapy Induced Oral Mucositis*	Evaluation of propolis on OM and radiotherapy-induced dysphagia.	Double-blind RCT	28 patients, mucositis & dysphagia were assessed by CTCAE & NCI.	Propolis 0.8 mg/ml 20 ml, 3x/day, swallowed, for 4 weeks.	Propolis is safe & effective in reducing OM and dysphagia. There was no difference in baseline characteristics.
	Mohd Hafiz Hamzah, MBBCH1, Irfan Mohamad, MD1, Muhamad	*Propolis mouthwash for preventing radiotherapy-induced mucositis in patients*	This study aims to test the effectiveness of 2.5% propolis mouthwash in	RCT	❑ The sample population was selected from patients diagnosed with NPC who visited the ORL-HNS	❑ Respondents in this study were randomly divided into an experimental group and a placebo group using a voting system.	❑ The results of this study showed that 17 patients completed the study with the

Database	Author, Country, Year	Article Title	Objective	Design	Samples & Measurements	Intervention	Results
	Yusri Musa, MD2, Nor Shahida Abd Mutalib, MBBS3 , Siti Azrin Ab Hamid, MBBS4 , Wan Adnan Wan Omar, MD5	*with nasopharyngeal carcinoma: A randomized control trial*	preventing radiotherapy-induced mucositis in head, mouth and neck cancer patients.		clinic who met the inclusion and exclusion criteria. Inclusion criteria were all patients diagnosed with NPC who were scheduled to undergo CCRT. Exclusion criteria were allergy to bee products, NPC stage T1 N0 M0, and age less than 18 years. All patients were evaluated biweekly for oral mucositis by the treating oncologist, who was also blinded, using World Health Organization (WHO) Oral Toxicity Scale and to prevent bias. All levels of mucositis were assessed and recorded at the second week sixth RT. The body weight of each patient was recorded at the beginning and at the end of treatment.	❑ The experimental group was given 2.5 ml of propolis mouthwash, and the placebo group was given normal saline mouthwash. ❑ All patients were given an instruction pamphlet. Mouthwashes (propolis and saline) were provided by the researchers and packaged in identical bottles labeled A and B. ❑ Propolis is diluted in water at 60°C until completely dissolved, and the volume is made up to 150 mL for gargling. The solution is stored in a regular refrigerator to prevent propolis fermentation. ❑ All patients were given a bottle of the product every week containing 150 mL of 2.5% propolis or normal saline according to their respective groups and were instructed to gargle with 7 mL (measured using the syringe provided) for 60 seconds and then spit it out. ❑ Gargling was performed three times a day and during RT from Monday to Friday, patients were instructed to gargle 30 minutes before starting RT, 30 minutes after completing RT, and then 6 hours after RT. ❑ On Saturday and Sunday, patients were instructed to gargle at specific times, namely 8 am, 3 pm, and 10	results of 10 patients using propolis mouthwash and seven patients using placebo mouthwash. The results obtained that the average mucositis score using propolis mouthwash compared to placebo in the second, fourth, and sixth weeks was 0.10 vs 1.14, 0.50 vs 2.00, and 1.20 vs 2.86, respectively, having differences between the two groups statistically significant ($p < 0.001$). ❑ Propolis mouthwash 2.5% is safe and effective in reducing the severity of mucositis in patients with head, oral, nasopharyngeal and neck cancer.

Database	Author, Country, Year	Article Title	Objective	Design	Samples & Measurements	Intervention	Results
						pm. And it was done for 6 weeks along with the RT protocol. ❑ RT Protocol. Given to assess patient compliance during the intervention then given a diary to record each time they perform the gargling procedure.	
Pubmed,ebsco	Patrícia Maria Fernandes, Pedro Luiz Rosalen, Diego Tetzner Fernandes, Emmanuel Dias-Neto Severino Matias Alencar, Bruno Bueno-Silva 6 Fábio de Abreu Alves and Márcio Ajudarte Lopes	*Brazilian organic propolis for prevention and treatment of radiation-related oral acute toxicities in head and neck cancer patients: A double-blind randomized clinical trial*	This study aims to determine the effectiveness of using BOP *(Brazilian organic propolis)* as a preventive and/or complementary therapy option. therapeutic options for radiotherapy-induced oral mucositis, dysphagia, dysgeusia, pain, and oral candidiasis and effects on proinflammatory cytokines and anti-inflammatory role	RCT	Sixty patients were included in this randomized, double-blind, controlled clinical trial, Controlled clinical trial. Patients were randomized to receive BOP suspension water or placebo during RT and all patients underwent low-level laser therapy as routine oral care. OM, dysphagia, and dysgeusia were assessed weekly according to the WHO and NCI scales. Pain related to OM was assessed using the Visual Analogue Scale and the presence or absence of oral candidiasis was assessed by intraoral examination. TNF-α and IL-1β protein levels from the oral mucosa were assessed by ELISA.	❑ Before the start of RT, each patient received an anonymous yellow spray bottle and neither the patient nor the professional was aware of the contents of the bottle. ❑ Intervention providers were instructed to apply the product topically to the oral mucosa at least 6 times a day, every day, including weekends from the first day of RT. Patients were encouraged to continue using the product until the last day of RT.	❑ Patients in the propolis group had lower mean OM scores, dysphagia, dysgeusia, and most patients reported moderate pain. ❑ Patients experiencing oral candidiasis in the propolis group had a lower number of episodes among patients using BOP ($p < 0.05$). In addition, the propolis group ❑ The BOP group showed significantly lower levels of IL-1β at baseline when compared to placebo patients ($p < 0.05$) and lower levels of TNF-α at the end of treatment ($p < 0.001$)
ProQuest	Ryoma Nakao and Takao Ueno	*Effects of oral moisturizing gel*	The aim of this study was to evaluate the	RCT	Twenty-seven ❑ subjects were recruited from outpatients	Intervention providers were randomly assigned to use oral gels	❑ The study showed that the number of Porphyromon

Database	Author, Country, Year	Article Title	Objective	Design	Samples & Measurements	Intervention	Results
		containing propolis follow head and neck radiotherapy: randomized controlled pilot trial	effects prevention and therapy of rebamipide mouthwash compared with *benzydamine HCl* in head and neck cancer patients undergoing radiotherapy alone or in conjunction with chemotherapy		undergoing radiotherapy of at least 50 Gy to the head and neck area.	with the following different ingredients: placebo, chlorhexidine, curry leaves, propolis, and turmeric. ❑ Before and after the intervention, oral symptoms were evaluated, and nine pathogens in saliva were also quantified using real-time PCR.	as gingivalis in saliva significantly decreased after treatment with propolis gel, but not after other treatments. ❑ Propolis gel treatment also relieved oral pain in all subjects who had oral pain at the start of the study. ❑ Topical application of propolis gel can not only reduce the carriage of P. gingivalis in saliva, but also relieve oral pain.
sciencedirect	Nayereh Darbanian, Monir Nobahar and Raheb Ghorbani	*Effect of propolis mouthwash on the incidence of ventilator-associated pneumonia in intensive care unit patients: A comparative randomized triple-blind clinical trial*	Taking into account the nature the right antioxidant and anti-inflammatory properties of curcumin, this study aims to to assess the effects of oral and topical curcumin formulations on ROM.	RCT	110 ICU patients in Imam-Hossein and Bahar (Shahroud) hospitals and Kowsar (Semnan) Hospital in Iran. The intervention group used 15 cc of 0.06% propolis mouthwash solution twice daily at 8 am and 4 pm for seven days. The control group used 15 cc of 0.2% chlorhexidine mouthwash at the same time and duration. Data were collected using a demographic questionnaire, APACHE II, Beck Oral Assessment Scale, and Modified Clinical	❑ This study involved 10 intervention providers in each of two groups, namely the intervention group (receiving propolis mouthwash) and the control group (receiving standard care). ❑ Patients were randomly assigned to the Control (Group A) or Intervention (Group B) control group. ❑ This study used a four-block randomization (A & B), with two individuals per group in each block. ❑ To ensure group balance, patients in opposing groups were selected based on similarity in age (within ± 5 years, with a maximum difference of 10 years) and gender	❑ Results There were no significant differences in demographic information, disease severity, and oral health between the two groups before and after the intervention (P > 0.05). ❑ The incidence of VAP in the intervention group compared to the control group was 10.9% vs 30.9% on the third day (P = 0.0166, 95% CI:

Database	Author, Country, Year	Article Title	Objective	Design	Samples & Measurements	Intervention	Results
					Pulmonary Infection Score (MCPIS).	difference of a maximum of 10 years), gender, and mechanical ventilation mode.	0.53-0.83 and RR = 0.35), 23.6% vs 43.6% on the fifth day (P = 0.0325 and 95% CI: 0.31-0.95 and RR = 0.54), and 25.5% vs 47.3% on the seventh day (P = 0.0224, 95% CI: 0.32-0.92, and RR = 0.54). Mann-Whitney showed that the incidence of VAP was significantly lower in the intervention group on the third, fifth, and seventh days. ❑ Conclusion Propolis mouthwash can be considered as an alternative to chlorhexidine mouthwash for ICU patients.
ScienceDirect	Mahboobe Dehghani, Mostafa Abtahi, Nadia Hasanzadeh, Zeinab Farahzad, Mohamad Noori, Meysam Noori	*Effect of Propolis mouthwash on plaque and gingiva indices over fixed orthodontic patients*	The aim of this study was to evaluate the effects of propolis mouthwash and chlorhexidine mouthwash on plaque and gingival index in	*RCT*	In this triple blind study, in total, 37 patients aged 15 to 35 years who had undergone orthodontic treatment Mouthwash containing Propolis or Chlorhexidine was randomly	❑ Propolis Mouthwash: 30 g of Propolis is mixed with 100 ml of distilled water and then mixed with a mixer at 30°C for 2 hours. The resulting Propolis mixing solution is 1% with a salt concentration of 0.25%, and together with	❑ The results of the study showed that the difference between the plaque index values (P <0.001), gingival index (P = 0.006) and

Database	Author, Country, Year	Article Title	Objective	Design	Samples & Measurements	Intervention	Results
			patients undergoing orthodontic treatment.		given to patients. The patients were asked to use the mouthwash twice a day after brushing their teeth for three consecutive weeks. Plaque, gingival and periodontal status indicators (PI, GI, CPI) were determined on Ramford teeth at the beginning and at the end of three weeks for each patient. Then the results were analyzed statistically.	turmeric essential oil and flavorings, a mouthwash is prepared. The prepared solution is put into 60 identical red bottles. ❑ Mixing Chlorhexidine Mouthwash: 0.2% Chlorhexidine mouthwash is mixed with clean water in a proportion of 3 parts mouthwash and 2 parts water, to obtain a 0.12% chlorhexidine solution. Then poured into 60 bottles. ❑ Respondents in the study were asked to use the mouthwash twice a day (morning and evening) after brushing their teeth for three consecutive weeks. ❑ Respondents were instructed to rinse with 15 mL of mouthwash for 1 minute followed by spitting out any remaining food and avoiding eating and drinking for up to 30 minutes and not to use any other mouthwash during the study period. Since each bottle contains 250 mL of mouthwash, ❑ three bottles of the same mouthwash were given to each patient. The protocol for using mouthwash was also given to the patients in written form. To avoid the effect of new variables, the subjects were asked to continue their usual daily toothbrushing method (toothbrush and dental floss)	periodontal index (P = 0.005) before and after administration of Propolis showed statistically significant results. ❑ The differences were statistically significant for all three plaque (P < 0.001), gingival (P = 0.001) and periodontal (P = 0.003) indices before and after the use of chlorhexidine mouthwash. ❑ It appears that Propolis mouthwash can be used as a suitable alternative in patients with orthodontic treatment without the side effects of chlorhexidine mouthwash.

Database	Author, Country, Year	Article Title	Objective	Design	Samples & Measurements	Intervention	Results
						during the study period. teeth and dental floss) during the study period. Then after three weeks of using mouthwash to re-evaluate the above-mentioned indices (plaque, gingival and periodontal index) on Ramford teeth. ❑ Data was recorded to compare conditions before and after using mouthwash.	

DISCUSSION

Oral mucosal injury or oral mucositis (OM) is an inflammation of the oral mucosa that frequently occurs as one of the most consistent side effects of anticancer drugs and radiation therapy regimens. OM can cause pain, difficulty eating and drinking, and a decline in the patient's quality of life. Therefore, various studies have been conducted to find effective and appropriate interventions to prevent and treat OM. However, no definitive intervention has yet been established for managing oral mucositis.Various types of treatments, both non-pharmacological and pharmacological, have been applied to prevent and manage oral mucositis. Management of OM involves the use of anti-inflammatory drugs, anesthetics, analgesics, antibiotics, cryotherapy, and mucosal coating agents. These approaches are discussed in the guidelines developed by the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer (MASCC/ISOO) and the International Society of Oral Oncology. Anti-inflammatory agents such as benzydamine and antimicrobial agents like chlorhexidine are used in the treatment of OM. Meanwhile, herbal agents act through various mechanisms, including antioxidant, analgesic, anti-inflammatory, antifungal, and antiseptic properties.

Various types of herbal agents used in patients undergoing chemotherapy include aloe vera, honey, curcumin, chitosan, and propolis. From eight studies, findings indicate that mouthwash containing propolis is superior to other herbal agents in reducing mucositis in cancer patients undergoing treatment. One study even found that propolis-based mouthwash was more effective in reducing gingival plaque (Dehghani et al., 2019).Several studies have shown that mouthwash containing propolis is effective in reducing OM symptoms such as pain, erythema, and ulceration. A study by Hamzah et al. (2022) involving patients with head and neck cancer undergoing chemotherapy found that propolis mouthwash effectively reduced mucositis, with 65% of patients in the propolis group completely healed by day 7. No significant side effects were reported, suggesting that propolis, as a natural agent, can effectively treat mucositis in cancer patients receiving chemotherapy.Another randomized controlled trial in head and neck cancer patients undergoing radiotherapy also demonstrated that water-based propolis extract significantly prevented and treated mucositis. In a double-blind clinical trial, the group using propolis showed lower mucositis scores compared to the placebo group. Additionally, propolis helped reduce the severity of mucositis and minimize weight loss during cancer treatment (Hamzah et al., 2022; Akhavan-Karbassi et al., 2016; Nakao & Ueno, 2021).

A similar study by Dastan et al. (2020) in patients undergoing radiotherapy showed a significant difference between the intervention group using propolis mouthwash and the placebo group. In the intervention group, no mucositis occurred during weeks three and four. Propolis contains various components, such as proteins, amino acids, vitamins, minerals, and flavonoids. Propolis mouthwash was found to be effective and safe in managing oral mucositis and dysphagia in cancer patients undergoing treatment.This aligns with a study by Bolouri et al. (2015), which evaluated the use of propolis mouthwash to prevent and reduce the severity of mucositis in head and neck cancer patients receiving radiotherapy. The study showed that patients using propolis mouthwash had significantly lower mucositis scores (based on NCI-CTC criteria) compared to the placebo group. Eight patients in the propolis group did not show any evidence of mucositis during radiotherapy. Although the study had limitations, such as a relatively small sample size, the results provide a strong basis for future research. Propolis is considered a safe and cost-effective preventive agent in managing radiation-induced oral mucositis.

Another study evaluated the effectiveness of Brazilian Organic Propolis (BOP) as a preventive and/or complementary therapy for radiation-induced oral mucositis, dysphagia, dysgeusia, pain, and oral candidiasis, as well as its effects on pro-inflammatory cytokines and anti-inflammatory roles. Patients in the propolis group had lower average OM scores, dysphagia, and dysgeusia, and most reported only moderate pain. Fewer episodes of oral candidiasis occurred in the propolis group ($p < 0.05$). Furthermore, the BOP group showed significantly lower levels of IL-1β from the beginning compared to the placebo group ($p < 0.05$) (Fernandes et al., 2022).Six studies examining the effectiveness of propolis in preventing and reducing chemotherapy- and radiation-induced oral mucositis reported no side effects such as burning sensation, altered taste, yellowing of teeth, or taste changes.

CONCLUSION

Following a literature review, several methods have been identified for managing oral mucositis in cancer patients undergoing chemotherapy and radiotherapy. The timing, method of application, and frequency of mouthwash use vary across studies. However, several articles indicate that the use of mouthwash can reduce oral mucositis in cancer patients undergoing these treatments. The selection of an appropriate intervention should be tailored to the individual condition and needs of each patient. Therefore, further research is needed to compare the effectiveness of various interventions and to develop an optimal protocol for the management of oral mucositis.

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