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SYSTEMATIC REVIEW OF LITERATURE

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THE EFFECT OF HERBAL APPROACHES ON ORAL MUCOSITIS IN ADULT CANCER PATIENTS - A SYSTEMATIC REVIEW OF NURSING STUDIES

O efeito das abordagens herbais na mucosite oral em pacientes adultos com câncer - uma revisão sistemática de estudos de enfermagem

El efecto de los enfoques herbales sobre la mucositis oral en pacientes adultos con cáncer - una revisión sistemática de estudios de enfermería

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ABSTRACT

Objective: to examine the effects of herbal approaches on oral mucositis in adult cancer patients. **Method:** systematic review following Cochrane guidelines, with a search for experimental and randomized studies from 2013 to 2023. English studies on herbal interventions in patients over 18 years were included. **Results:** eight studies that used herbal interventions to treat oral mucositis were evaluated. The herbs tested included aloe vera, althaea root, turmeric, chamomile, grape vinegar, rose water, fruit/vegetable juice, and mulberry extract. The interventions varied in frequency and duration but showed positive results, reducing oral mucositis intensity, pain, and other symptoms. Some interventions were as effective as conventional treatments like chlorhexidine. **Conclusion:** the research suggests that herbal approaches can be beneficial in managing oral mucositis in cancer patients, but more studies are needed to confirm these results.

Descriptors: Herbal interventions; Mucositis; Systematic review.

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RESUMO

Objetivo: examinar os efeitos das abordagens herbais na mucosite oral em pacientes adultos com câncer. **Método:** revisão sistemática seguindo as diretrizes da Cochrane, com uma busca por estudos experimentais e randomizados entre 2013 e 2023. Foram incluídos estudos em inglês sobre intervenções herbais em pacientes com mais de 18 anos. **Resultados:** foram avaliados oito estudos que usaram intervenções herbais para tratar a mucosite oral. As ervas testadas incluíram aloe vera, raiz de althaea, cúrcuma, camomila, vinagre de uva, água de rosas, suco de frutas/vegetais e extrato de amoreira. As intervenções variaram em frequência e duração, mas mostraram resultados positivos, reduzindo a intensidade da mucosite oral, dor e outros sintomas. Algumas intervenções foram tão eficazes quanto tratamentos convencionais como a clorexidina. **Conclusão:** a pesquisa sugere que abordagens herbais podem ser benéficas no manejo da mucosite oral em pacientes com câncer, mas mais estudos são necessários para confirmar esses resultados.

Descritores: Intervenções herbais; Mucosite; Revisão sistemática.

RESUMEN

Objetivo: examinar los efectos de los enfoques herbales en la mucositis oral en pacientes adultos con cáncer. **Método:** revisión sistemática siguiendo las directrices de Cochrane, con una búsqueda de estudios experimentales y aleatorizados entre 2013 y 2023. Se incluyeron estudios en inglés sobre intervenciones herbales en pacientes mayores de 18 años. **Resultados:** se evaluaron ocho estudios que utilizaron intervenciones herbales para tratar la mucositis oral. Las hierbas probadas incluyeron aloe vera, raíz de althaea, cúrcuma, manzanilla, vinagre de uva, agua de rosas, jugo de frutas/verduras y extracto de moras. Las intervenciones variaron en frecuencia y duración, pero mostraron resultados positivos, reduciendo la intensidad de la mucositis oral, el dolor y otros síntomas. Algunas intervenciones fueron tan eficaces como tratamientos convencionales como la clorhexidina. **Conclusión:** la investigación sugiere que los enfoques herbales pueden ser beneficiosos para el manejo de la mucositis oral en pacientes con cáncer, pero se necesitan más estudios para confirmar estos resultados.

Descriptorios: Intervenciones herbales; Mucositis; Revisión sistemática.

INTRODUCTION

Cancer is a disease caused by abnormal cell growth that can lead to metastasis in different parts of the body.¹ Cancer was the second leading cause of death worldwide in 2018, being responsible for an estimated 9.6 million deaths, or one in every six deaths (2). In 2020, with a total of 18 million diagnoses, cancer is one of the most prevalent and disabling diseases of this century.³⁻⁴ Chemotherapy and radiotherapy are used as main or adjunctive treatments in cancer management and cause many complications, including destruction of epithelial cells.^{1,5}

Chemotherapy represents the most effective neoplastic drugs to treat malignancies. Chemotherapy has specific toxicities and side effects. Oral mucositis is one of the side effects associated with chemotherapy.⁶ While chemotherapy prevents the proliferation and development of cancer cells, it also damages the mucosal barrier by suppressing the growth and maturation of epithelial cells.⁷ Radiotherapy can also damage normal cells while eliminating cancerous cells, causing destruction of taste buds, function loss in salivary glands and oral mucositis.⁸

Oral mucositis is a common complication of cancer treatment and is a weakening factor in many cases.¹ Mucositis is inflammation and ulceration of the mucous membrane covering the gastrointestinal system from the oral cavity to the anus. If this process occurs in the oral and oropharyngeal parts, it is defined as oral mucositis.⁵ Mucosal ulcers may first appear as redness of the mucosa and develop into mucosal ulcers later in the treatment. The prognosis of oral mucositis varies according

to the treatment regimen, nutritional status, kidney and liver function.⁹

Oral mucositis is common in 20-40% of individuals receiving chemotherapy and in almost all individuals receiving radiotherapy.¹⁰ Cancer treatment-induced oral mucositis occurs 3-14 days after treatment and lasts 3-4 weeks, while radiotherapy-induced oral mucositis lasts 3-12 weeks.^{9,11} Mucositis may occur in any part of the oral cavity, but most commonly affects non-keratinized areas such as the buccal mucosa, soft palate and floor of the oral cavity.¹² Oxidative stress and inflammation play a role in the pathophysiology of cancer therapy-induced oral mucositis. Cancer treatments increase cytokines with the formation of high levels of reactive oxygen species. Cytokines affect the inflammation process, aggravating tissue damage and leading to ulcerations.¹³ Signs and symptoms of oral mucositis include dry mouth, edema, pain, taste changes, odynophagia, dysphagia and hoarseness.^{14,15}

Oral mucositis causes decreased nutrient intake, communication difficulties, decreased self-esteem, impaired pain-related comfort and psychosocial problems. Such problems may lead to decreased quality of life, treatment delays, increased treatment costs and incomplete treatment.^{1,5-6} Oral mucositis-induced pain and dysphagia may prevent adequate nutrition and lead to dehydration, weight loss, systemic infections and even aspiration.^{10,14,16} Such complications result in intravenous infusion, parenteral nutrition, opioid and barbiturate use, and in severe cases, gastric tube and gastrostomy feeding.¹⁷

Management of oral mucositis is a difficult process. Howe-

ver, the effects of complications may be reduced with early diagnosis and treatment. Oral mucositis has a significant impact on an individual's survival by influencing the treatment process.^{9,18} Due to the complications caused, developing a standardized nursing approach to the diagnosis and treatment of oral mucositis is important.¹ The Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology¹⁹ emphasized basic oral care and patient education in the guidelines for the management of cancer treatment-related oral mucositis.

Nurses have important responsibilities in evidence-based care and symptom management, to identify, prevent and improve the risk factors of oral mucositis.^{10,20} Through their close contact with patients, nurses have a unique position to recognize, assess and manage the symptoms of oral mucositis and provide preventive strategies and interventions.¹⁸ Nurses need to have sufficient knowledge and skills by following current developments in order to prevent the occurrence of mucositis and to provide effective care.²¹

Management of oral mucositis includes oral hygiene care with antimicrobial agents, sodium bicarbonate and chlorhexidine mouthwash solutions, the use of anti-inflammatory, topical and systemic analgesic drugs, antioxidants, cryotherapy, herbal approaches, honey and probiotics.²² Despite the many methods used in the prevention and treatment of oral mucositis, effective management has not been achieved. Every intervention has its advantages and disadvantages.¹

Less side effects compared to chemical medicines have led to the need for further research on interventions containing natural components.¹⁸ Some patients refuse to use chemical mouthwashes because of the irritation of tooth color, taste and oral cavity. This irritation becomes difficult to tolerate in individuals with suppressed immune systems due to treatment.^{9,17} Therefore, natural and herbal products are considered as alternatives in the management of oral mucositis.⁹

Herbal products and other natural compounds have gained more popularity in recent years than synthetic compounds in the management of many chronic diseases.²³ Herbal interventions have positive benefits on side effects related to cancer treatments.²⁴ Herbal interventions, used since ancient times, are one of the methods used for the management of oral mucositis. Interest in the therapeutic effects of herbal interventions has increased due to low side effects^{14,17} Phytochemicals highly present in plants have antioxidant, analgesic, antifungal, anti-septic, anticarcinogenic and anti-inflammatory effects.^{16,25} Due to these effects, herbal interventions can be safely used traditionally in oral and dental health.²⁴ This systematic review aims to discuss the effects of herbal interventions on oral mucositis in adult cancer patients.

OBJECTIVE

The aim of this systematic review is to investigate the effects of herbal interventions on oral mucositis in adult cancer

patients.

RESEARCH QUESTION

Are herbal interventions effective in the management of oral mucositis in adult cancer patients?

METHOD

RESEARCH DESIGN

This systematic review was prepared according to Cochrane guidelines.²⁶

RESEARCH STRATEGY

The studies included were determined by the PICOS method.²⁶

P(Population): The sample of the study consisted of studies involving the herbal interventions in the management of oral mucositis for individuals with cancer, regardless of gender, race, socioeconomic class, and including individuals aged 18 years and older.

I(Intervention): Research involving the herbal interventions in the management of oral mucositis in adult cancer patients was investigated.

C(Comparator): The effectiveness of herbal interventions was compared to routine care or other treatments.

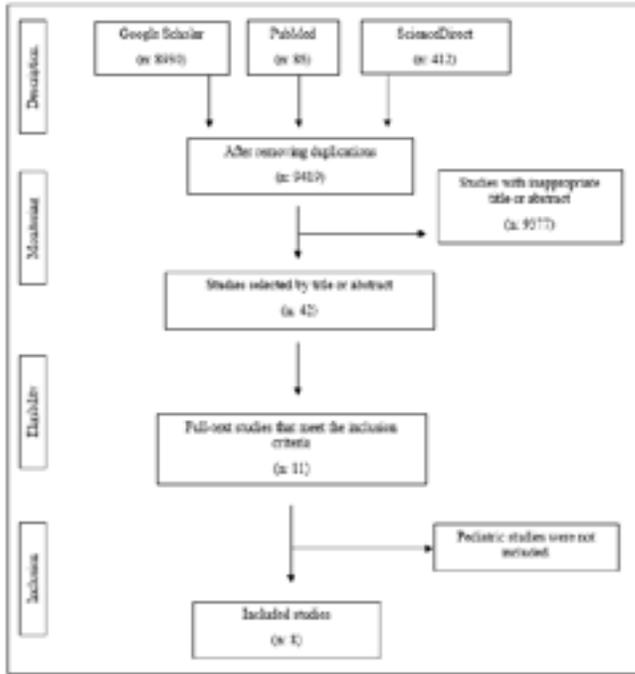
O(Outcome): The effects of herbal interventions on oral mucositis prevention, oral mucositis severity, oral mucositis-induced pain, dry mouth and weight gain were investigated.

S(Study Design): Randomized controlled and experimental studies in English with full text available were included in the review.

DETERMINATION OF STUDIES

Before the literature review, databases and keywords were determined. Articles published in English between 2013 and 2023 were included in the review. In this direction, "Google Scholar, PubMed, ScienceDirect" databases were searched. The keywords "oral mucositis, nursing, randomized" were used in the search. The number of studies reached after the search was categorized according to databases and shown in the PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) flowchart (Figure 1).

Figure 1 - Flowchart of studies included in the systematic review (PRISMA-P flowchart).



INCLUSION CRITERIA

Randomized controlled and experimental nursing studies in English, in that herbal interventions were applied to individuals with cancer, and included patients aged 18 years and over, regardless of gender, race, socioeconomic class, and full text was available, were included in the review without limitation of sample size.

EXCLUSION CRITERIA

Studies not reporting results of herbal interventions for oral mucositis in adult cancer patients and studies that were not randomized controlled or experimental were not included.

ASSESSMENT THE RISK OF BIAS

The risk of bias was assessed by the two researchers using the Cochrane risk of bias assessment tool. The risk of bias is categorized into three levels: low, uncertain and high (Figure 2).

Figure 2 - Risk of bias assessment: “+/-low risk of bias “; “?/unclear risk of bias”; “-/-high risk of bias “

	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Nasouri et al. (2016), Iran	?	?	-	-	-	?	-
Chorbari et al. (2018), Iran	-	?	-	-	-	?	-
Chorbari et al. (2019), Iran	?	-	-	-	-	?	-
David and Shree (2019), India	-	?	?	?	?	?	-
Abdelhussien et al. (2020), Egypt	-	-	-	-	?	?	-
Mirzadad et al. (2020), Iran	-	?	-	?	-	?	-
Chang et al. (2022), Taiwan	-	?	?	?	-	?	-
Karabey et al. (2022), Turkey	-	?	?	?	?	?	-

Cochrane risk of bias criteria includes selection bias, performance bias, identification bias, missing bias, and other biases(27). Parameters indicating that any study has a low risk of bias are the use of a random number table or computerized randomization, the use of opaque or sealed envelopes to conceal randomization information, blinding of researchers and participants, and blinding of outcome assessment. Parameters indicating a high risk of bias are randomization by preference, absence or impairment of blinding, and results being affected by the lack of blinding. In case of insufficient information when determining the risk of bias, it is referred to as uncertain risk.28

The 8 studies included in the systematic review were assessed for risk of bias. Of the 8 studies, 5 had a low selection bias, 4 had a low performance bias, 3 had a low identification bias, 7 had a low loss bias and all had low other bias (Figure 2).

RESULTS

Table 1 presents the 8 studies included in the systematic review. The results were investigated in terms of the study characteristics, herbal interventions, frequency of interventions, measurement tools and the outcomes of the interventions.

STUDY	STUDY DESIGN	SAMPLE	INTERVENTIONS	MEASUREMENT TOOLS	RESULTS
Mansouri et al. (2016), Iran	Randomized controlled	Lymphoma and leukemia patients receiving chemotherapy Intervention (n: 32) Control (n:32)	Intervention group: Aloe vera and routine care Control group: Normal saline Normal saline: Routine mouthwashes containing chlorhexidine and nystatin. Mouthwash 2 minutes with 5 mL of solution 3 times a day for 2 weeks. No oral intake for 30 minutes afterwards.	Visual Analog Scale (VAS) WHO Oral Mucositis Grading Scale Stomatitis examination and pain control on days 1, 3, 5, 7 and 14.	It was found that stomatitis intensity and pain decreased in the intervention group compared to the control group. Significant differences were observed between the two groups except for the first day.
Ghorbani et al. (2018), Iran	Triple-blind randomized controlled	Cancer patients with chemotherapy-induced stomatitis Intervention (n: 25) Control (n:25)	Intervention group: Half of routine mouthwash and 8% concentration of althaea root extract. Control group: Routine mouthwash. -Contents of routine mouthwash: Lidocaine, Dexamethasone, Sucralfate and Diphenhydramine. Mouthwash for 3 minutes with 15 mL of solution 4 times a day for 14 days.	Visual Analog Scale (VAS) Pain control on days 1, 7 and 14.	A decrease in pain scores was observed in both groups on days 7 and 14. -The decrease in pain scores in the experimental group was found to be more significant than in the control group.
Ghorbani et al. (2019), Iran	Double-blind randomized controlled	Cancer patients with chemotherapy-induced stomatitis Intervention (n: 25) Control (n:25)	Intervention group: Half of routine mouthwash and 8% concentration of althaea root extract. Control group: Routine mouthwash. -Contents of routine mouthwash: Lidocaine, Dexamethasone, Sucralfate and Diphenhydramine. -Mouthwash for 3 minutes with 15 mL of solution 4 times a day for 14 days.	WHO Oral Mucositis Grading Scale -Stomatitis severity control on days 1, 7 and 14.	A decrease in stomatitis severity was observed in both groups on days 7 and 14. -Stomatitis severity decreased more in the experimental group than in the control group.
David and Shree (2019), India	Real-experimental comparative	Mucositis patients receiving radiation therapy Intervention (n: 30) Control (n:30)	Intervention group: Mouthwash (5 mL turmeric and 50 mL water). Control group: Sodium bicarbonate mouthwash. -Mouthwash for 1 minute 2 times a day for 1 week.	-National Cancer Institute Mucositis Scoring -At week 2, assess the severity of oral mucositis.	-Turmeric mouthwash was found to be more effective than sodium bicarbonate in reducing the severity of oral mucositis.
AbdElwadoud et al. (2020), Egypt	Quasi-experimental	Patients with head and neck cancer, receiving radiotherapy and having mucositis Intervention (n: 30) Control (n: 30)	Intervention group: Therapeutic oral gel and Chamomile gel. Control group: Therapeutic oral gel. -Using 3 times a day 1 hour before a meal for 6 months and then stopping oral intake for 1 hour.	National Cancer Institute Mucositis Scoring -Patient Reported Oral Mucositis Symptoms Scale -Numeric Pain Rating Scale -Assessment every 6 weeks.	There was an increase in the degree of oral mucositis in both groups, but this increase was significantly lower in the intervention group. -The results in pain and symptoms reported by patients were significantly different in the intervention group.

Afrasiabi-far et al. (2020), Iran	Randomized controlled	Cancer patients receiving chemotherapy or admitted to the oncology clinic Intervention (n: 30) Control (n: 30)	Intervention group: Combined solution of grape vinegar and rose water. Control group: Chlorhexidine. -Mouthwash for 1 minute with 15 mL 3 times a day for 14 days. Oral intake stopped for 1 hour.	WHO Oral Mucositis Grading Scale -Assessment on days 7, 14 and 21.	Chlorhexidine mouthwash and grape vinegar-rose water combination mouthwash both reduced chemotherapy-induced oral mucositis. -The therapeutic effect of the combined solution of grape vinegar-rose water is similar to chlorhexidine.
Chang et al. (2022), Taiwan	Quasi-experimental	Head and neck cancer patients receiving radiotherapy Intervention (n: 25) Control (n: 24)	Intervention group: Routine care, Nutritional counseling, Fruit/vegetable juice. Control group: Routine care and nutritional counseling. -Fruit/vegetable juice contents: Carrot, beet root, celery, cucumber, alfalfa sprouts, tomato, apple, guava, orange, lemon, pineapple and wolfberry. -600 mL per day, 5 days a week, for 6 weeks.	WHO Oral Mucositis Grading Scale -European Organization for Research and Treatment of Cancer Head and Neck Cancer Module -Body Mass Index -Assessment at beginning and at the end of 6 weeks.	Changes in body weight were not significantly different between the two groups. -The incidence of oral mucositis at week 6 of chemotherapy was significantly lower in the intervention group than in the control group.
Karabey et al. (2022), Turkey	Randomized controlled	Cancer patients receiving chemotherapy Intervention (n: 20) Control (n:20)	Intervention group: Black Mulberry Extract. Mouthwash for 1 minute with 5 mL 3 times a day for 15 days. Control group: Sodium bicarbonate mouthwash. Mouthwash for 30 seconds with 10 mL 3 times a day for 15 days.	Oral Evaluation Guidelines -Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) Late Radiation Morbidity Scoring Scheme -Weight follow-up -Assessment at day 1, 7 and 15.	There was a significant decrease in mucositis and dry mouth in both groups. -There was a significant increase in weight follow-up in the intervention group compared to the control group.

CHARACTERISTICS OF STUDIES

The studies included in the systematic review consisted of English language studies that met the inclusion criteria. The studies were all randomized controlled or experimental research.

Various herbal interventions such as aloe vera, althea flower, turmeric, chamomile, grape vinegar, rose water, fruit/vegetable juice and black mulberry extract have been used in the studies. Studies have investigated the effect of herbal interventions on the severity and pain of oral mucositis, dry mouth, and body weight in individuals with cancer.

HERBAL INTERVENTIONS

Studies that herbal interventions were used in the management of oral mucositis in individuals with cancer were investigated in terms of the content of the interventions. In the studies reviewed, aloe vera, althea flower, turmeric, chamomile, grape vinegar, rose water, fruit/vegetable juice and black mulberry herbs were used.

Herbal methods were used in the form of mouthwash solu-

tions, gels and oral intake. In most of the studies, routine care, nutritional counseling and therapeutic gel interventions were provided to both groups, but those in the intervention group were additionally provided with herbal methods.^{14,16-18,29} In other studies, chlorhexidine, nystatin, sodium bicarbonate solutions and normal saline were used in the control groups, and herbal interventions were used in the intervention groups.^{9,15,30}

FREQUENCY OF INTERVENTIONS

Most studies lasted for 2 weeks and the frequency of intervention was three and four times a day. The intervention times vary between 30 seconds and 3 minutes, and the amount of solution used varies between 5 mL and 15 mL.^{9,14,15,17,29} Some studies stopped oral intake for 30 minutes or 1 hour after each intervention.^{9,29}

In David and Shree's³⁰ study, 55 mL of solution was used for mouthwash 2 times a day for one minute for 1 week. AbdElwadoud et al.⁽¹⁸⁾ investigated the effects of oral gel interventions one hour before a meal 3 times a day for 6 months. Chang et al.¹⁶ studied 600 mL oral intake 5 days a week for 6 weeks.

MEASUREMENT TOOLS

Visual Analog Scale (VAS) and Numeric Pain Scale were used to assess oral mucositis pain in studies.^{14,18,29} The numeric pain scale developed by McCaffery and Beebe³¹ has a score range of 0-10. VAS, another measurement tool used in pain assessment, easy to use, valid and reliable. The scale is in the form of a 10 cm ruler, with 0 representing no pain and 10 representing excruciating pain.^{14,29}

The WHO Oral Mucositis Grading Scale was used to assess oral mucositis in most of the studies.^{9,16,17,29} The scale is classified as 0 points no stomatitis, 1 point erythema without pain and sores, dry mouth, 2 points erythematous sores, 3 points large and erythematous sores, 4 points mucosal bleeding, diffuse inflammation and complete restriction of oral intake.^{16,29}

The National Cancer Institute Mucositis Scoring was used to determine the severity of oral mucositis in two of the studies.^{18,30} In the five-point Likert scale developed by the National Cancer Institute³²; 0 points is classified as no oral mucositis, 1 point as mild, 2 points as moderate, 3 points as severe, and 4 points as life-threatening oral mucositis.

AbdElwadoud et al.¹⁸ used the Patient-Reported Oral Mucositis Symptoms Scale to assess symptoms of oral mucositis. The scale developed by Kushner et al.³³ is used to assess the impact of oral mucositis on oral health. It is a 10-item visual analog scale that questions conditions such as difficulty in eating solid/hard foods, mouth pain and taste changes. In each item, a point between 0 and 100 is marked and an increase in the score indicates an aggravation of the symptom.

Chang et al.¹⁶ used the European Organization for Research and Treatment of Cancer (EORTC) Head and Neck Cancer module (QLQ-H&N35) to assess oral health. The module developed by the EORTC Quality of Life Group³⁴ includes items to assess oral pain and dryness. The grading is based on a four-point Likert scale.

Karabey et al.¹⁵ used the Oral Evaluation Guidelines and RTOG/EORTC Late Radiation Morbidity Scoring Scheme to assess oral mucositis. The Oral Assessment Guide developed by Eilers et al.³⁵ consists of five sections assessing the lips, mucous membranes, tongue, gingiva and saliva. The score range is 8-24 and as the score increases, the risk of developing oral mucositis increases. The score range of the RTOG/EORTC Late Radiation Morbidity Scoring Scheme used to assess dry mouth is 0-5.

Weight and body mass index were measured in studies investigating the changes in body weight.^{15,16}

IMPACT OF INTERVENTIONS

Mansouri et al.²⁹ investigated the effects of aloe vera mouthwash on oral mucositis and found that stomatitis intensity and pain decreased in the intervention group compared to the control group. They found that there were changes in the parameters investigated from the first day. Ghorbani et al.^{14,17} investigated the effects of althea root on oral mucositis in two separate studies. They determined that the pain score and severity

of stomatitis were lower in the intervention group compared to the control group at 7 and 14 days. David and Shree³⁰ investigated the effect of turmeric-containing mouthwash solution and sodium bicarbonate solution on the severity of oral mucositis. In the study, turmeric was significantly more effective than sodium bicarbonate in reducing the severity of oral mucositis. AbdElwadoud et al.¹⁸ investigated the effects of chamomile gel on oral mucositis and found that the severity of oral mucositis increased in both groups, but this increase was less in the intervention group. They observed that the reporting of symptoms related to pain and oral mucositis was significantly lower in the intervention group. Afrasiabifar et al.⁹ investigated the effect of grape vinegar and the rose water combined solution on oral mucositis and obtained the same results as the chlorhexidine treated group. They reported that chlorhexidine and a combined solution of grape vinegar/rose water had the same therapeutic effect on oral mucositis.

Chang et al.¹⁶ investigated the effect of fruit/vegetable juice on the oral mucositis incidence and body weight and determined that rich fruit/vegetable juice helped a significant decrease in the oral mucositis incidence in the 6th week of chemotherapy compared to the control group. They observed that fruit/vegetable juice had no significant difference in body weight between the two groups. Karabey et al.¹⁵ investigated the effects of the black mulberry extract on oral mucositis, dry mouth and body weight and reported a more significant weight gain in the intervention group. They found that there was no significant difference between the severity of oral mucositis and dry mouth between both groups.

DISCUSSION

This systematic review analyzed the effects of herbal interventions containing aloe vera, althaea root, turmeric, chamomile, grape vinegar, rose water, fruit/vegetable juice and black mulberry on oral mucositis. Aloe vera has been used as a topical remedy for skin conditions for 2000 years. Aloe vera has softening, moisturizing, anti-inflammatory effects on the skin and has no side effects.^{29,36} Mansouri et al.²⁹ found that aloe vera was more effective in oral mucositis intensity and pain than routine treatment. When the literature is analyzed, there are studies showing that aloe vera is effective in preventing oral mucositis or has similar effects with standard care.³⁷⁻³⁹ Another herbal method whose effect on the severity and pain level of oral mucositis was investigated was mouthwash solution containing althaea root. Althea root is one of the medicinal plants used in many conditions such as gingivitis, dry throat, severe cough, constipation, regulation of blood glucose and cholesterol levels. Natural compounds in the root of the althea root have antiplatelet, anti-inflammatory and antibacterial effects.^{14,17} Ghorbani et al.^{14,17} determined that althea root reduced the pain and severity of oral mucositis in their studies. When the literature is reviewed, it is seen that there are a limited number of studies investigating the effect of althea root on oral mucositis.^{14,17}

Turmeric was another herbal method in which the effect of oral mucositis was studied. Turmeric is one of nature's most effective healing resources recommended to protect against the harmful effects of radiation and chemotherapy without reducing their effectiveness.³⁰ Turmeric has antioxidant, analgesic, anti-inflammatory, antiseptic, antimicrobial and anticarcinogenic effects.⁴⁰ David and Shree³⁰ reported that turmeric was more effective than sodium bicarbonate in reducing the severity of oral mucositis. There are studies in the literature that associate turmeric with a decrease in oral mucositis severity and pain scores and a decrease in oral function loss.^{41,42}

Chamomile is a plant that has long been used in traditional and herbal treatment and shows anti-inflammatory, antibacterial, spasmolytic and antifungal effects due to the compounds it contains.¹⁸ Chamomile has been tested for toxicity and found safe for mucosal surface.⁴³ Studies show that the use of chamomile in different forms (topical gel, cryotherapy) is effective in preventing oral mucositis and reducing pain caused by oral mucositis.^{43,44}

Other herbal interventions that have been studied for their effect on oral mucositis include grape vinegar and rose water. Natural vinegar has antibacterial, antihypertensive, antihyperglycemic and antioxidant effects, while rose water has anti-inflammatory and antimicrobial effects with the natural compounds it contains.⁹ There are limited studies investigating the effect of rose and vinegar on oral mucositis.^{9,45} Ameri et al.⁴⁵ determined that the use of roses as mouthwash reduces the risk of oral mucositis and improves quality of life.

Another of the herbal methods studied is black mulberry. Black mulberry is a plant with antifungal and strong antimicrobial properties that has important effects especially in the healing of mouth and dental wounds.⁴⁶ In the literature, there are studies showing that black mulberry has positive effects on the prevention of oral mucositis and reduction of dry mouth^{46–48}, while there are also studies showing that it has no effect.⁴⁹

CONCLUSION

There is no established standard of care and treatment for the prevention and management of oral mucositis. Considering the negative effects of cancer treatments on individuals, healthcare professionals should have sufficient knowledge in the management of possible problems. The main principle in oral mucositis care should be the use of evidence-based practices as in all nursing interventions.

Herbal interventions have less side effects than chemical methods and have high anti-inflammatory and antioxidant effects. In the studies investigated in the systematic review, it was found that the herbal methods applied had positive effects on the severity of oral mucositis, pain, dry mouth, oral mucositis-induced symptoms and body weight. In all of the studies, herbal interventions had positive effects on at least one of the parameters investigated.

The effects of different plants were investigated in the studies. In order to reach a clearer conclusion about the possible effects and side effects of the plants studied, the findings need

to be supported by more clinical studies. The reason for analyzing only nursing studies within the scope of the review is to be able to limit the herbal oral mucositis interventions, which are very extensively in the literature, and to investigate the interventions of nurses, who play an important role in the management of oral mucositis. The fact that only nursing studies were analyzed could be considered among the limitations of the review.

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REFERENCES

1. ArbabiSarjou A, Khamar M, Sasanpour P, Kiani F. The Effect of Self-Care Training on the Severity of Oral Mucositis in Breast Cancer Patients Undergoing Chemotherapy. *Med-Surg Nurs J*. [Internet]. 2021 [cited 2024 apr 25];10(4):e123386. Available from <https://doi.org/10.5812/msnj.123386>
2. World Health Organization (WHO). Cancer. [Internet]. 2019 [cited 2024 apr 25]. Available from: <https://www.who.int/health-topics/cancer>
3. Mohammadi F, Oshvandi K, Kamallan SR, Khazaei S, Ranjbar H, Ahmadi-Motamayel F, vd. Effectiveness of Sodium Bicarbonate and Zinc Chloride Mouthwashes in the Treatment of Oral Mucositis and Quality of Life in Patients with Cancer Under Chemotherapy. *Nurs Open*. Mayis [Internet]. 2022 [cited 2024 apr 25];9(3). Available from: <https://doi.org/10.1002/nop2.1168>
4. Global World Cancer Research Fund International. Global Cancer Data by country. [Internet]. 2023 [cited 2024 apr 25]. Available from: <https://www.wcrf.org/cancer-trends/global-cancer-data-by-country/>
5. Askarifar M, Lakdizaji S, Ramzi M, Rahmani A, Jabbarzadeh F. The Effects of Oral Cryotherapy on Chemotherapy-Induced Oral Mucositis in Patients Undergoing Autologous Transplantation of Blood Stem Cells: A Clinical Trial. *Iran Red Crescent Med J*. [Internet]. 2016 [cited 2024 apr 25];18(4):e24775. <https://doi.org/10.5812/ircmj.24775>
6. Ali YM, El-Kady MS, Ali HS, Abdelatief DAA, Abdel-slam SN. Effect of Educational Guidelines on Reducing Chemotherapy Induced Oral Mucositis Based on Patients' Needs Assessment. *Int J Res Pharm Sci*. [Internet]. 2020 [cited 2024 apr 25];11(SPL4). Available from: <https://doi.org/10.26452/ijrps.v11iSPL4.4514>

7. Kostak MA, Semerci R, Eren T, Kocaaslan EN, Yıldız F. Effects of Oral Health Care Education on the Severity of Oral Mucositis in Pediatric Oncology Patients. *Turk J Oncol*. [Internet]. 2020 [cited 2023 apr 25];35(4). Available from: <https://doi.org/10.5505/tjo.2020.2366>
8. Ghorbani F, Yazdanian M, Tahmasebi E, Izadi M, Mofid B, Varpaei HA. Effect of Ozonated Water on Oral Mucositis and Pain Induced by Head and Neck Radiotherapy: A Cross-Sectional Study. *Arch Neurosci*. [Internet]. 2021 [cited 2023 apr 25];8(4):e118914. Available from: <https://doi.org/10.5812/ans.118914>
9. Afrasiabifar A, Dekhordi NJ, Mosavi A, Mozaffari MAN, Bani ZAB. Oral Mucositis: Examining the Combined Solution of Grape Vinegar and Rose Water Versus Chlorhexidine Mouthwash. *Clin J Oncol Nurs*. [Internet]. 2020 [cited 2023 apr 25];24(6). Available from: <https://doi.org/10.1188/20.CJON.E71-E78>
10. Avcı Ş, Sarı HY. Effect of an Evidence-Based Nursing Intervention on the Diagnosis of Oral Mucositis in the Pediatric Stem Cell Transplant Unit. *Asia-Pac J Oncol Nurs*. [Internet]. 2019 [cited 2023 apr 25];6(3). Available from: https://doi.org/10.4103/apjon.apjon_5_19
11. Toygar I, Yeşilbalkan ÖU. Determining the Non-Pharmacological Methods Using to Cope with Radiation-Related Oral Mucositis in Patients with Head and Neck Cancer. *Nurs Pract Today*. [Internet]. 2019 [cited 2023 apr 25];6(3). Available from: <https://publish.kne-publishing.com/index.php/NPT/article/view/1254>
12. Bai RR. Effectiveness of Oral Ice Cube Application on Prevention of Oral Mucositis Among Cancer Patients Who Receive Chemotherapy. *Innov J Nurs Heal*. [Internet]. 2019 [cited 2023 apr 25];5(3). Available from: <https://doi.org/10.31690/ijnh/39>
13. Chan CWH, Law BMH, Wong MMH, Chan DNS, Ng MSN, So WKW, vd. Oral Mucositis Among Chinese Cancer Patients Receiving Chemotherapy: Effects and Management Strategies. *Asia Pac J Clin Oncol*. Nisan [Internet]. 2021 [cited 2023 apr 25];17(2). Available from: <https://doi.org/10.1111/ajco.13349>
14. Ghorbani MS, Taghadosi M, Shariat A, Akbari H. Effects of Althaea Root Extract on Alleviating Chemotherapy-Induced Stomatitis Pain: A Randomized Controlled Clinical Trial. *J Client-Centered Nurs Care*. [Internet]. 2018 [cited 2023 apr 25];4(1). Available from: <https://www.sid.ir/FileServer/JE/50002120180105>
15. Karabey T, Karagözoğlu Ş, Aygün N, Sümer Z. The Effect of Oral Care with Black Mulberry Extract on Oral Mucositis, Dry Mouth, and Weight Gain in Patients with Cancer. *Clin J Oncol Nurs*. [Internet]. 2022 [cited 2023 apr 25];26(6). Available from: <https://doi.org/10.1188/22.CJON.636-642>
16. Chang HP, Huang MC, Lei YP, Chuang YJ, Wang CW, Sheen LY. Phytochemical-Rich Vegetable and Fruit Juice Alleviates Oral Mucositis During Concurrent Chemoradiotherapy in Patients with Locally Advanced Head and Neck Cancer. *J Tradit Complement Med*. [Internet]. 2022 [cited 2023 apr 25];12(5). Available from: <https://doi.org/10.1016/j.jtcme.2022.03.004>
17. Ghorbani MS, Taghadosi M, Akbari H, Sharifi M. Effect of Hydroalcoholic Extract of Althaea Officinalis Root on Improving Chemotherapy-Induced Stomatitis: A Randomized, Double-Blind, Clinical Trial. *Nurs Midwifery Stud*. [Internet]. 2019 [cited 2023 apr 25];8(1). Available from: https://doi.org/10.4103/nms.nms_42_18
18. AbdElwadoud AM, Hassanein SM, El-Deen DS, Abdou I. Using Chamomile for Alleviating Oral Mucositis Among Patients with Head and Neck Cancer Receiving Radiotherapy. *Egypt Nurs J*. [Internet]. 2019 [cited 2023 apr 25];16(3). Available from: https://doi.org/10.4103/ENJ.ENJ_12_20
19. Lalla RV, Bowen J, Barasch A, Elting L, Epstein J, Keefe DM, vd. MASCC/ISOO Clinical Practice Guidelines for the Management of Mucositis Secondary to Cancer Therapy. *Cancer*. [Internet]. 2020 [cited 2023 apr 25];120(10). Available from: <https://doi.org/10.1002/cncr.28592>
20. Kara H, Arıkan F, Kartöz F, Şahin AFK. Nurse-Led Oral Mucositis Management: Impact on Health Outcomes of Patients Receiving Radiotherapy for Head and Neck Cancer and Lung Cancer: A Prospective Study. [Internet]. 2022 [cited 2023 apr 25]; [HTTPS://DOI.ORG/10.21203/rs.3.rs-1734361/v1](https://doi.org/10.21203/rs.3.rs-1734361/v1)
21. Harman M, Ovayolu N, Ovayolu ÖU. The Effect of Three Different Solutions on Preventing Oral Mucositis in Cancer Patients Undergoing Stem Cell Transplantation: A Non-Randomized Controlled Trial: A Turkish Study. *J Pak Med Assoc*. [Internet]. 2019 [cited 2023 apr 25];69(6). Available from: <https://acikerisim.medipol.edu.tr/xmlui/handle/20.500.12511/776>
22. Badr LK, El Asmar R, Hakim S, Saad R, Merhi R, Zahreddine A, vd. The Efficacy of Honey or Olive Oil on the Severity of Oral Mucositis and Pain Compared to Placebo (standard Care) in Children with Leukemia Receiving Intensive Chemotherapy: A Randomized Controlled Trial (RCT). *J Pediatr Nurs*. [Internet]. 2023 [cited 2023 apr 25];70:e48-53. Available from: <https://doi.org/10.1016/j.pedn.2022.12.003>

23. Ambili R, Ramadas K, Nair LM, Raj D, Nazeer F, George PS, vd. Efficacy of a Herbal Mouthwash for Management of Periodontitis and Radiation-Induced Mucositis—a Consolidated Report of Two Randomized Controlled Clinical Trials. *J Ayurveda Integr Med.* [Internet]. 2023 [cited 2023 apr 25];14(6). Available from: <https://doi.org/10.1016/j.jaim.2023.100791>
24. Safarzadeh S, Shirban F, Bagherniya M, Sathyapalan T, Sahebkar A. The Effects of Herbal Medicines on Cancer Therapy Oral Mucositis: A Literature Review. *Phytother Res. Ocak* [Internet]. 2022 [cited 2023 apr 25];36(1). Available from: <https://doi.org/10.1002/ptr.7308>
25. Baharvand M, Jafari S, Mortazavi H. Herbs in Oral Mucositis. *J Clin Diagn Res JCDR.* [Internet]. 2017 [cited 2023 apr 25];11(3). Available from: <https://doi.org/10.7860/JCDR/2017/21703.9467>
26. Cochrane Library. Cochrane Handbook for Systematic Reviews of Interventions. [Internet]. 2023 [cited 2023 apr 25]. Available from: <https://training.cochrane.org/handbook/current>
27. Cochrane Library. Rob 2: A Revised Cochrane Risk-of-Bias Tool for Randomized Trials | Cochrane Bias. [Internet]. 2019 [cited 2023 apr 25]. Available from: <https://methods.cochrane.org/bias/resources/rob-2-revised-cochrane-risk-bias-tool-randomized-trials>
28. Kalav S, Çetin AA, Bektaş H. The Effect of Oral Hygiene Practices in Patients with Stroke: Systematic Review. *Turk Klin J Nurs Sci.* [Internet]. 2020 [cited 2023 apr 25];12(3). Available from: <https://doi.org/10.5336/nurses.2020-74729>
29. Mansouri P, Haghighi M, Beheshtipour N, Ramzi M. The Effect of Aloe Vera Solution on Chemotherapy-Induced Stomatitis in Clients with Lymphoma and Leukemia: A Randomized Controlled Clinical Trial. *Int J Community Based Nurs Midwifery.* [Internet]. 2016 [cited 2023 apr 25];4(2). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4876780/>
30. David MPR, Shree MKT. Effectiveness of Turmeric Mouthwash and Sodium Bicarbonate Mouthwash to Reduce Oral Mucositis among Patient Undergoing Radiation Therapy. *Sch Int J Tradit Complement Med.* [Internet]. 2019 [cited 2023 apr 25];2(7). <https://doi.org/10.36348/SIJTCM.2019.v02i07.001>
31. McCaffery M, Beebe A. The Numeric Pain Rating Scale Instructions. *Pain Clin Man Nurs Pract.* [Internet]. 1989 [cited 2023 apr 25]. Available from: <http://nperesource.casn.ca/wp-content/uploads/2017/02/Numeric-Pain-Rating-Scale-Instructions.pdf>
32. Bjarnason GA, MacKenzie RG, Nabid A, Hodson ID, El-Sayed S, Grimard L, vd. Comparison of Toxicity Associated with Early Morning Versus Late Afternoon Radiotherapy in Patients with Head-and-Neck Cancer: A Prospective Randomized Trial of the National Cancer Institute of Canada Clinical Trials Group (HN3). *Int J Radiat Oncol Biol Phys.* [Internet]. 2009 [cited 2023 apr 25];73(1). Available from: <https://doi.org/10.1016/j.ijrobp.2008.07.009>
33. Kushner JA, Lawrence HP, Shoval I, Kiss TL, Devins GM, Lee L, vd. Development and Validation of a Patient-Reported Oral Mucositis Symptom (PROMS) Scale. *J Can Dent Assoc.* [Internet]. 2008 [cited 2023 apr 25];74(1):p59-59j. Available from: <https://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope=site&authtype=crawler&jrn1=07098936&AN=30006141&h=90yvGQW-9sUKXaPJ%2Fbfdg%2FgBlUbQYiOfyH6m%2FAD-1NtS3OzXHILHi%2FQGeiNzQmy7%2B8LDXOx%2FmLxE%2FP4iQx5Ijg%3D%3D&crl=c>
34. Bjordal K, Ahlner-Elmqvist M, Tolleson E, Jensen AB, Razavi D, Maher EJ, vd. Development of a European Organization for Research and Treatment of Cancer (EORTC) Questionnaire Module to be Used in Quality of Life Assessments in Head and Neck Cancer Patients. *Acta Oncol. Ocak* [Internet]. 1994 [cited 2023 apr 25];33(8). Available from: <https://doi.org/10.3109/02841869409098450>
35. Eilers J, Berger AM, Petersen MC. Development, Testing, and Application of the Oral Assessment Guide. *Oncology Nursing Society.* [Internet]. 1988 [cited 2023 apr 25]. Available from: <https://experts.nebraska.edu/en/publications/development-testing-and-application-of-the-oral-assessment-guide>
36. Guberti M, Botti S, Caffarri C, Cavuto S, Savoldi L, Fusco A, vd. Efficacy and Safety of a Colostrum- and Aloe Vera-Based Oral Care Protocol to Prevent and Treat Severe Oral Mucositis in Patients Undergoing Hematopoietic Stem Cell Transplantation: A Single-Arm Phase II Study. *Ann Hematol. Ekim* [Internet]. 2022 [cited 2023 apr 25];101(10). Available from: <https://doi.org/10.1007/s00277-022-04934-4>
37. Alkhouli M, Laflouf M, Alhaddad M. Efficacy of Aloe-Vera Use for Prevention of Chemotherapy-Induced Oral Mucositis in Children with Acute Lymphoblastic Leukemia: A Randomized Controlled Clinical Trial. *Compr Child Adolesc Nurs.* 02 Ocak [Internet]. 2021 [cited 2023 apr 25];44(1). Available from: <https://doi.org/10.1080/24694193.2020.1727065>
38. Karbasizade S, Ghorbani F, Darestani NG, Mansouri-Tehrani MM, Kazemi AH. Comparison of Therapeutic

- Effects of Statins and Aloe Vera Mouthwash on Chemotherapy Induced Oral Mucositis. *Int J Physiol Pathophysiol Pharmacol*. [Internet]. 2021[cited 2023 apr 25];13(4). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8446774/>
39. Sahebamee M, Mansourian A, Hajimirzamohammad M, Zadeh MT, Bekhradi R, Kazemian A, vd. Comparative Efficacy of Aloe Vera and Benzydamine Mouthwashes on Radiation-Induced Oral Mucositis: A Triple-Blind, Randomised, Controlled Clinical Trial. *Oral Health Prev Dent*. [Internet]. 2015 [cited 2023 apr 25];13(4). Available from: <https://doi.org/10.3290/j.ohpd.a33091>
40. Normando AGC, De Meneses AG, De Toledo IP, Borges GÁ, De Lima CL, Dos Reis PED, vd. Effects of Turmeric and Curcumin on Oral Mucositis: A Systematic Review. *Phytother Res. Mayıs*. [Internet]. 2019 [cited 2023 apr 25];33(5). Available from: <https://doi.org/10.1002/ptr.6326>
41. Soni TP, Gupta AK, Sharma LM, Singhal H, Sharma S, Gothwal RS. A Randomized, Placebo-Controlled Study to Evaluate the Effect of Bio-Enhanced Turmeric Formulation on Radiation-Induced Oral Mucositis. *Orl*. [Internet]. 2022 [cited 2023 apr 25];84(2). Available from: <https://doi.org/10.1159/000516577>
42. Thomas PL, Kang HK, Rishi KS. 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 Nurs*. [Internet]. 2023 [cited 2023 apr 25];46(1). Available from: <https://doi.org/10.1097/NCC.0000000000001149>
43. Elhadad MA, ElNegoumy E, Taalab MR, Ibrahim RS, Elsaka RO. The Effect of Topical Chamomile in the Prevention of Chemotherapy Induced Oral Mucositis: A Randomized Clinical Trial. *Oral Dis. Ocak*. [Internet]. 2022 [cited 2023 apr 25];28(1). Available from: <https://doi.org/10.1111/odi.13749>
44. Reis PEDD, Ciol MA, de Melo NS, Figueiredo PT de S, Leite AF, Manzi N de M. Chamomile Infusion Cryotherapy to Prevent Oral Mucositis Induced by Chemotherapy: A Pilot Study. *Support Care Cancer*. [Internet]. 2016 [cited 2023 apr 25];24. Available from: <https://doi.org/10.1007/s00520-016-3279-y>
45. Ameri A, Heydarirad G, Choopani R, Poshtmahi S, Ameri P, Talebi F, vd. Sumac-Rose Water Mouthwash Versus Benzydamine to Prevent Radiation-Induced Oral Mucositis in Head and Neck Cancers: A Phase Ii Randomized Trial. *J Cancer Res Clin Oncol*. [Internet]. 2023 [cited 2023 apr 25]. Available from: <https://doi.org/10.1007/s00432-023-04687-1>
46. Korkut S, Karadağ S, Çınar SL. The Effect of Oral Care with Black Mulberry Syrup on Oral Mucositis in Patients with COPD: A Mixed Study. *Altern Ther*. [Internet]. 2021 [cited 2023 apr 25]. Available from: <http://www.alternative-therapies.com/oa/pdf/6430.pdf>
47. Doğan P, Tarhan M, Kürklü A. Effectiveness of Black Mulberry Molasses in Prevention of Radiotherapy-Induced Oral Mucositis: A Randomized Controlled Study in Head and Neck Cancer Patients. *The Journal of Alternative and Complementary Medicine*. [Internet]. 2023 [cited 2023 apr 25];11(2). Available from: <https://doi.org/10.1089/acm.2016.0425>
48. Fischer L. Black Mulberry Extract Shows Efficacy in Oral Mucositis Management for Patients Receiving Chemotherapy. *Oncol Nurs News*. [Internet]. 2022 [cited 2023 apr 25];NA-NA. Available from: <https://go.gale.com/ps/i.do?p=HRCA&sw=w&issn=&v=2.1&it=r&id=GALE%-7CA762612137&sid=googleScholar&linkaccess=abs>
49. Sarı SY, Beduk Esen CS, Yazici G, Yuce D, Cengiz M, Ozyigit G. Do Grape and Black Mulberry Molasses Have an Effect on Oral Mucositis and Quality of Life in Patients with Head and Neck Cancer? *Support Care Cancer*. [Internet]. 2022 [cited 2023 apr 25];30. Available from: <https://doi.org/10.1007/s00520-021-06411-6>
50. Ebrahim AA, Ahmed ES, Eltayeb AA, Sayed EH. Role of Chlorhexidine in Preventing Mucositis Among Ventilated Children at Pediatric Intensive Care Unit. *Assiut Sci Nurs J*. [Internet]. 2022 [cited 2023 apr 25];10(28.). Available from: <https://doi.org/10.21608/ASNJ.2022.121442.1323>