# The Effect of Propolis Tablet on Oral Mucositis Caused by Chemotherapy

## Propolis Tabletinin Kemoterapiye Bağlı Gelişen Oral Mukozit Üzerine Etkisi

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**ABSTRACT**

**Background:** Oral mucositis is defined as oral mucosal inflammation in cancer patients that is caused by chemotherapy and/or radiotherapy. Propolis is a natural product produced by bees and has antimicrobial, antioxidant, and anti-inflammatory effects. Therefore, considering the anti-inflammatory properties of Propolis, the aim of this study is to evaluate the efficacy of Propolis tablet on oral mucositis caused by chemotherapy.
**Materials and Methods:** In this randomized, double-blinded, placebo-controlled study, 50 patients were enrolled in the study, and samples were taken from patients on Folfox chemotherapy regimen with colon cancer who were admitted to the Oncology Center of Imam Khomeini Hospital in Sari. The patients were then divided into two groups of 25. The first group received 50 mg Propolis tablets as 2 tablets per day for 21 days and the second group received placebo. All patients were examined by oral medicine specialist after initial examination, weekly and for 3 weeks, and the severity of mucositis was recorded according to WHO criteria. Data analysis was performed in SPSS ver. 22 software using T test and Mann-Whitney and Kruskal-Wallis tests.
**Results:** The age range of the participants in the study was between 26-72 years. In the intervention group 13 women (52%) and 12 men (48%) and in the control group 13 women (52%) and 12 men (48%) participated .In this study, there was a significant difference in the mean of oral mucositis severity in the Propolis group compared to placebo group**.** In the intervention group, oral mucositis grade was significantly lower in the 2nd and 3rd follow up sessions than in the placebo group ($p < 0.05$). No negative complications were reported by patients.
**Conclusion:** This clinical trial study showed that Propolis tablet could play an important role in preventing and improving the oral mucositis caused by chemotherapy.

**Key Words:** Propolis, mucositis, chemotherapy

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**ÖZET**

**Amaç:** Oral mukozit, kemoterapi ve/veya radyoterapinin neden olduğu kanser hastalarında oral mukozal inflamasyon olarak tanımlanır. Propolis, arılar tarafından üretilen ve antimikrobiyal, antioksidan ve anti-inflamatuar etkileri olan doğal bir üründür. Bu nedenle, Propolis'in antiinflamatuar özellikleri göz önüne alınarak, bu çalışmanın amacı, Propolis tabletinin kemoterapinin neden olduğu oral mukozit üzerindeki etkinliğini değerlendirmektir.
**Yöntem:** Bu randomize, çift-kör, plasebo kontrollü çalışmada, 50 hasta çalışmaya alındı ve Sari'deki Imam Khomeini Hastanesi Onkoloji Merkezine başvuran kolon kanseri olup Folfox kemoterapi rejiminde olan hastalardan örnekler alındı. Hastalar daha sonra 25'er iki gruba ayrıldı. İlk grup 21 gün boyunca günde 2 tablet olarak 50 mg Propolis tableti aldı ve ikinci grup plasebo aldı. Tüm hastalar ilk muayeneden sonra, haftalık ve 3 hafta boyunca diş hekimi tarafından muayene edildi ve WHO kriterlerine göre mukozit şiddeti kaydedildi. Veri analizi, T testi, Mann-Whitney ve Kruskal-Wallis testleri kullanılarak SPSS ver.22 yazılım ile yapıldı.
**Bulgular:** Çalışmaya katılanların yaş aralığı 26-72 yıl arasındaydı. Müdahale grubunda 13 kadın (% 52), 12 erkek (% 48) ve kontrol grubunda 13 kadın (% 52),12 erkek (% 48) bu çalışmaya katılmıştır. Propolis grubunda plasebo grubuna göre oral mukozit şiddeti açısından istatistiksel olarak anlam vardı. Girişim grubunda oral mukozit derecesi 2. ve 3. takip seanslarında plasebo grubuna göre anlamlı olarak düşüktü ($p < 0.05$). Hastalar tarafından hiçbir olumsuz komplikasyon bildirilmedi.
**Sonuç:** Bu klinik çalışma çalışması, Propolis tabletinin kemoterapinin neden olduğu oral mukozitin önlenmesinde faydalı ve önemli bir rol oynayabileceğini göstermiştir.

**Anahtar Sözcükler:** Propolis, mukozit, kemoterapi

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## INTRODUCTION

Oral mucositis is defined as oral mucosal injury in people with cancer, which is caused both by chemotherapy and radiotherapy in patients with head and neck cancer. Mucositis is a painful and debilitating side effect, which makes nutrition of patients difficult (1).

In mucositis, levels of IL6, IL1β and TNFα cytokines are elevated and increased inflammatory immune cells' infiltrates in submucosal can be seen (2).

Clinical findings include erythema, edema and allergy associated with painful ulcers and mucosal hemorrhage (1). There is a link between the progression of mucositis and microorganisms (3), in which Staphylococcus aureus was isolated from patients undergoing chemotherapy, and fungal microorganisms have also been shown to be effective in the development of oral mucositis, the most common of which is candidiasis (4). Currently, oral mucosal management is essentially supportive treatment, including good oral hygiene, avoiding irritating and abrasive substances, using mouthwash, local anesthetic substances and systemic analgesics (5-7). For thousands of years, natural products have been used for treatment. Many of them have medical, pharmacological and dental aspects such as anti-microbial, anti-inflammatory, anesthetic, anti-viral and anti-oxidant compounds (8). Finding a safe substance, which increases the effect of chemotherapy with reduced side effects, is very valuable and useful. Recently, medications used in traditional medicine have been re-considered. One of the cases that has recently been considered for its antimicrobial and anti-inflammatory properties is Propolis (9, 10). Propolis is a resin material collected by a honeycomb from various plant sources and is mixed with the enzymes of the salivary glands of the bee and wax that the bees use them to repair the hive walls and protect colony against diseases (1). Propolis contains more than three hundred natural compounds, including polyphenol, phenolic aldehyde, amino acids, steroids, quinones, terpenes and inorganic compounds**.** Propolis has shown a wide range of biological and pharmacological benefits such as antimicrobial, antioxidant, anti-inflammatory, immune regulator, anti-tumor, anti-cancer, anti-ulcer aspects with conservatory effects on liver, heart and nerves (11, 12). Since Propolis contains components such as zinc and iron, it is considered important for synthesis of collagen (13). Propolis stimulates the immune system as an anti-inflammatory agent by enhancing phagocytic and cellular immune activity and enhancing the effects of healing on epithelial tissues (14). Anti-inflammatory activity of Propolis on oral mucosa in the treatment of denture induced stomatitis (1) and also in the treatment of recurrent aphthous stomatitis and eosinophilic ulcer is remarkable (15, 16). The beneficial effect of Propolis against oxidative stress induced by anticancer drugs doxorubicin and vinblastine has been proven on rabbits (17). Antibacterial, antifungal and antiviral activity of Propolis for Streptococcus viridans (18) and Candida albicans (19) and herpes simplex virus (20) have been shown to commonly cause secondary infection in patients undergoing chemotherapy (21, 22). Therefore, due to the anti-inflammatory properties of Propolis, and considering the fact that in animal studies, Propolis has been shown to be effective in the prevention and treatment of mucositis due to radiotherapy, and so far the effect of this drug on the prevention and treatment of chemotherapy induced mucositis has not been studied, the aim of this study was to evaluate the efficacy of Propolis tablet on oral mucositis caused by chemotherapy.

## MATERIALS and METHODS

The present study is a double-blind clinical trial. The target population was selected from patients with similar cancer and under the same chemotherapy regimen that were referred to the outpatient chemotherapy department of Imam Khomeini Hospital in Sari in March 2017. Before starting the study and intervention, the RCT code was obtained (IRCT2017060933722N2).

Selected patients had colon cancer and the chemotherapy regimen prescribed for them was the Folfox diet (oxaloplatin, lacorin, fluoracillin), which often caused mucositis. The chemotherapy cycle was repeated every three weeks and was subjected to chemotherapy for two consecutive days in each cycle.

Inclusion criteria were people with the same cancer (colon) and the same chemotherapy regimen that were able to co-operate, had no acute liver and kidney disease, and also with no smoking and alcohol consumption. In addition, patients should not use any other treatment for oral mucositis during the course of the program.

Exclusion criteria were also considered as a failure to complete the course of the patient's pills, or to become more acutely ill, and to have an allergy to Propolis.

To determine the sample size, the results of a study by Dr. Nafiseh Saghafi et al. in 2015 entitled "Comparative study on the efficacy and complications of Propolis and chemotherapy with chemotherapy alone in neo-adjuvant therapy of ovarian cancer" were used, which had a mean volume of mass before treatment of 114.39 with a standard deviation of 78.19 and after intervention of 52.9 with a standard deviation of 47.76 (9). Therefore, the sample size with a confidence level of 95%, a test power of 90%, and a two-way test range were calculated using the formula for comparing the two averages in the G-Power software, equal to 50 people (25 in the intervention group and 25 in the control group).

The selected patients were randomly divided into two groups: intervention and control. Since the subjects in the intervention group had to take two tablets of Propolis daily and the duration of the treatment was three weeks, the number of required Propolis tablets was 1050, which Purchased from Soren Tak Tous Pharmaceutical Company in Mashhad and became available.

Control subjects should also take two placebo tablets or placebo per day during treatment, which is estimated at 1050 pills. The placebo was purchased from Soren Tak Tous Pharmaceutical Company in Mashhad. 50 cans, each containing 42 pills of Propolis or placebo, on each can labeled the name of pills or "Propolis 50mg" and pills' usage order "please eat 2 pills daily with your meals" was given to the implementers of the plan. Since the design is double blinded, the cans were encoded by the pharmaceutical company, in which 25 cans received code A and 25 cans received code B. To be mentioned patients participating in the project and examiners, had no information on how the cans were encoded. At the end of the project, and after analyzing the data by the statistical consultant, information was provided to the implementers about the coding of the cans by the pharmaceutical company.

All patients were examined by an oral medicine specialist before the onset of treatment by using a mirror and a flashlight and the oral mucosa was examined and the inclusion criteria with the absence of mucositis in all patients was confirmed. Subsequently, patients in the end of each week for three weeks was evaluated and examined for mucositis index. Therefore, the number of examination sessions for each patient was considered four times.

A clinical examination was performed to evaluate oral mucositis based on the WHO index. Accordingly, the results were categorized into five categories (0 without mucositis, 1 erythema without ulcers, redness, pain, sensitivity, 2 erythema, redness, ulcers, and little ability to eat solids, 3 ulcerous but require fluid regimen and 4 no edible feeding) (23).

After obtaining informed consent and observing the principles and ethical points, people entered the plan and received treatment. Two groups of Propolis tablets were given to the intervention group for three weeks, and two groups of placebo tablets were given to the control group at that same time, and patients were evaluated at the beginning of the study at the end of each week by an examiner and the mucositis criteria was evaluated.

Data analyse was done in SPSS Ver. 22 software. The normal distribution was performed by Kolmogorov-Smirnov test. The variables were described using frequency, mean and standard deviation.

For comparison before and after intervention, paired t test or its nonparametric equivalents (Kruskal Wallis) and for comparison after intervention, between two groups of intervention and control, independent t test or its nonparametric equivalents (Mann-Whitney test), repeatability analysis of variance or Friedman and Chi-Square were used.

## RESULTS

In this study, 50 patients were divided into two groups: intervention (n = 25) and control (n = 25). In the intervention group 13 women (52%) and 12 men (48%) and in the control group 13 women (52%) and 12 men (48%) participated. Totally, 52% of patients were female and 48% were male. There was no statistically significant difference between them (p = 1.000).

The age range of 50 patients was 26-75 years old. The mean age in the intervention group was 47.68 years and in the control group was 53.68 years. This difference was not statistically significant (p = 0.066).

Two groups were evaluated for systemic disease. In the intervention group 5 patients (20%) and in the control group 10 patients (40%) had systemic disease, and the remaining patients (80% of patients in the intervention group and 60% of the control group) did not have a systemic underlying disease. This difference was not statistically significant between the two groups (p = 0.127).

Two groups were evaluated for the use of other drugs, in the intervention group 6 patients (24%) and in the control group 7 patients (28%) used other drugs, and the remaining patients (76% of patients in the intervention group and 72% of patients in the control group) did not use any other drug. This difference was not statistically significant (p = 0.750).

In the initial examination (before the start of treatment), the oral mucosal status of the patients in both groups was at equal level and the statistical difference between them was not significant. Because the conditions for entry into the study were that patients had no oral mucositis at the beginning of the project, or in other words, all patients were registered for the severity of mucositis according to WHO criteria with zero grade.

Seven days after the start of chemotherapy, at the end of the first week or the first follow up session, the average severity of mucositis was 0.98 according to the WHO criteria in the intervention group and in the control group it was 1.16. Based on independent T-test analysis, this difference was not statistically significant (p = 0.312). Fourteen days after the start of chemotherapy, at the end of the second week or the second follow up session, the average severity of mucositis was 0.8 according to the WHO criteria in the intervention group. And in the control group it was 1.4. Based on independent T-test, the difference between the two groups was statistically significant (p = 0.027). Twenty one days after the start of the treatment, at the end of the third week or the third follow up session, the average severity of mucositis was 0.52 in the intervention group and 1.00 in the control group, based on the WHO criteria. Based on independent T-test, the difference between the two groups was statistically significant (p = 0.039). Comparison of mucositis severity in the first, 2nd and 3rd follow up sessions between the control and intervention group were shown in table 1.

**Table 1**. Comparison of mucositis severity in the first, 2nd and 3rd follow up sessions between the control and intervention groups.

| Day and Group | Numbers | Average | Standard Deviation | p-value |
|---|---|---|---|---|
| Intervention group Day 7 | 25 | 0.9200 | 0.75939 | 0.312 |
| Control group | 25 | 1.1600 | 0.80000 | |
| Intervention Group Day 14 | 25 | 0.8000 | 0.91287 | 0.027 |
| Control Group | 25 | 1.4000 | 0.95743 | |
| Intervention Group Day 21 | 25 | 0.5200 | 0.71414 | 0.039 |
| Control Group | 25 | 1.0000 | 0.86603 | |

Based on repeated analysis of variance, the comparison of the mean mucositis severity during the period of the examination sessions was significant in both the control and intervention groups (p = 0.001) but the significance level of the comparison of the mean of mucositis severity during the period of the examination sessions between both the control and intervention group was at borderline (p = 0. 050). All result for comparison of the average mucositis during the period of the examination sessions within the control and intervention groups and between the control and intervention groups were shown in table 2.

**Table 2.** Comparison of the average mucositis during the period of the examination sessions within the control and intervention groups and between the control and intervention groups.

| | Day 7 Average | Standard Deviation | Day 14 Average | Standard Deviation | Day 21 Average | Standard Deviation | p-value within | p-value between |
|---|---|---|---|---|---|---|---|---|
| Intervention Group | 0.9200 | 0.75939 | 0.8000 | 0.91287 | 0.5200 | 0.71414 | 0.001 | 0.050 |
| Control Group | 1.1600 | 0.80000 | 1.4000 | 0.95743 | 1.0000 | 0.86603 | 0.001 | |

Comparison of the frequency of mucositis grades in patients participating in the plan during different examinations between two intervention and control groups based on chi-square analysis was not significant at any of the follow up sessions (p> 0.05). All results for Comparison of mucositis grade in different days between both the intervention and control groups were shown in table 3.

**Table 3**- Comparison of mucositis grade in different days between both the intervention and control groups.

| Variable (Grade) | | Net number | Intervention Group | | Control Group | | Level of significance (chi-square) |
|---|---|---|---|---|---|---|---|
| | | | Number | Percent | Number | Percent | |
| Day 7 | 0 | 13 | 8 | 61.5 | 5 | 38.5 | 0.612 |
| | 1 | 23 | 11 | 47.8 | 12 | 52.2 | |
| | 2 | 13 | 6 | 46.2 | 7 | 53.8 | |
| | 3 | 1 | 0 | 0 | 1 | 100 | |
| Day 14 | 0 | 17 | 12 | 70.6 | 5 | 29.4 | 0.165 |
| | 1 | 15 | 7 | 46.7 | 8 | 53.3 | |
| | 2 | 14 | 5 | 35.7 | 9 | 64.3 | |
| | 3 | 4 | 1 | 25 | 3 | 75 | |
| Day 21 | 0 | 23 | 15 | 65.2 | 8 | 34.8 | 0.198 |
| | 1 | 17 | 7 | 41.2 | 10 | 58.8 | |
| | 2 | 9 | 3 | 33.3 | 6 | 66.7 | |
| | 3 | 1 | 0 | 0 | 1 | 100 | |

Comparison of the graph showing the average intensity of mucositis in the intervention and control group during the period of the participation in the plan indicates that in all follow up sessions, the mean mucositis severity was lower in the intervention group than in the control group. The results of this survey are shown in Figure 1. Also Comparison of average mucositis severity between examination sessions in the intervention and control group were shown separately in figures 2 and 3.

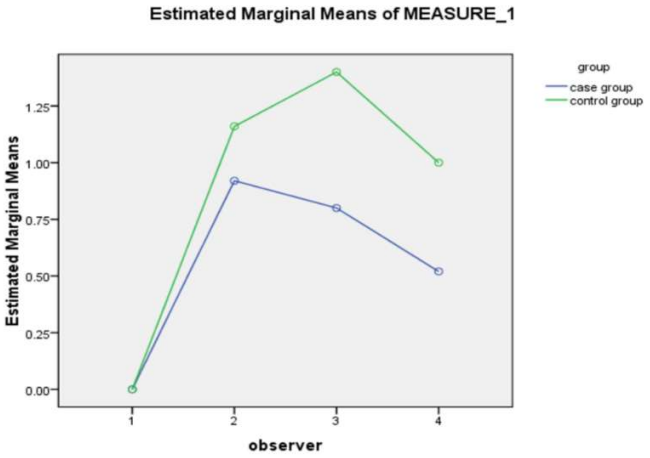


**Figure 1.** Comparison of average mucositis severity between the intervention and control groups.

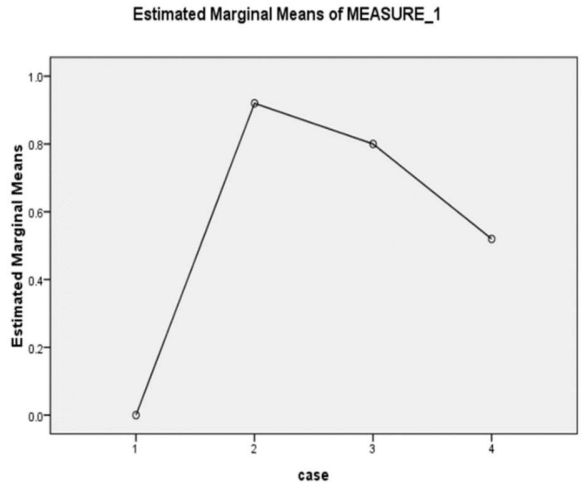


**Figure 2.** Comparison of average mucositis severity between examination sessions in the intervention group.

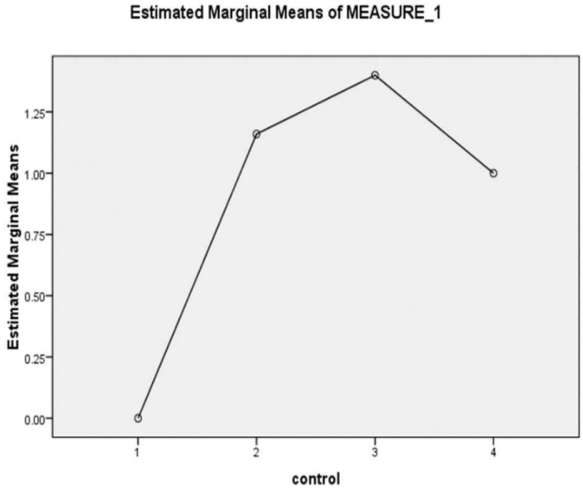


**Figure 3.** Comparison of average mucositis severity between examination sessions in the control group.

## DISCUSSION

The age range of the participants in the study was between 26-72 years. In the intervention group 13 women (52%) and 12 men (48%) and in the control group 13 women (52%) and 12 men (48%) participated .In this study, there was a significant difference in the mean of oral mucositis severity in the Propolis group compared to placebo group**.** In the intervention group, oral mucositis grade was significantly lower in the 2nd and 3rd follow up sessions than in the placebo group. (P <0.05). No negative complications were reported by patients.

Ulcerative oral mucositis is a debilitating and painful condition that results from the toxicity associated with the amount and dose of cancer treatment. Oral mucositis is also defined as oral mucosal injury in patients with oral cancer that is caused both by chemotherapy and radiotherapy in patients with cancer (1).

Propolis has anti-inflammatory effects in relation to large amounts of C-Artepillin in it. On the other hand, benefits of antimicrobial Propolis is of the presence of flavonoids. Noticing the complex composition of Propolis, making the activity of each composition in a separated manner is difficult, while researches have shown that all Propolis composites have synergistic effects (5).

In the present study, the mean of mucositis severity in follow up sessions 1 to 3 in the intervention group was 0.92, 0.8 and 0.52, respectively, indicating a decrease in the intensity of mucositis by continuing the use of Propolis tablet. These results indicate that the severity of mucositis symptoms in the patients in the study group gradually decreased and the trend was improving. Studies done by Blury and Akhavan are in line with this study (24, 25).

Average mucositis intensity of the control group in the first follow up was 1.16 and in the second fallow up was 1.4 and in the third fallow up was equal to 1.00. Therefore, in the control group, the severity of mucositis symptoms in the second follow up was increased compared to the first follow up session, and patients in the second week indicated more severe mucositis than the first week. In 3$^{rd}$ follow up, the average mucositis severity in the control group was reduced compared to 1$^{st}$ follow up and 2$^{nd}$ one. This reduction can be attributed to the self-healing process of oral mucositis.

Often, oral mucositis appears between the seventh and 14th day of chemotherapy, and this is when medications reduce huge amounts of white blood cells. Mucositis usually drops one or two weeks after the end of treatment (26).

In this study, the patients in the control group at the third follow up session, 21 days after the onset of treatment, showed a significant decrease in the severity of mucositis compared to the first follow up (7 days after the onset of treatment). So far, research on the effects of Propolis on oral mucositis from chemotherapy has examined other forms of Propolis drugs such as mouthwashes and mucoadhesive gel and mucosal adherent, while most researches focused on oral mucositis from radiotherapy. The present study is categorized in early studies on the effects of Propolis tablets on oral mucositis caused by chemotherapy in humans.

The term mucositis in the late 1980s was used to describe the oral mucosal inflammation caused by radiotherapy (in 80% of patients), chemotherapy (in 40% -80% of patients), and bone marrow transplantation (in over 75% of patients); a phenomenon as a manifestation of leukopenia was introduced. Today, Oral mucositis is now recognized as the most serious non-hematological complication of cancer treatment (27).

In the present study, 50 patients who participated in the study showed a total of 74% of patients with a degree of mucositis during the course of the program, which was 34% of the studied group and 40% of the control group.

Also, in the intervention group (n = 25), 32% of the patients did not show any symptoms of oral mucositis, whereas in a study by Vladimir and his colleagues, 80% of patients in the mucoadhesive Propolis gel group (n = 25) did not show oral mucositis symptoms (5).

This difference can be due to the more effective use of focal Propolis compared to systemic Propolis. That study examined the effect of 5% Mucoadhesive Propolis gel on oral mucositis caused by radiotherapy. It was shown in this study that Mucoadhesive Propolis gel is able to control inflammation and oral infection (5).

The results from other studies have also confirmed the anti-inflammatory and antimicrobial effects of Propolis. The present study from the view of the effect of Propolis tablets on reducing the incidence of mucositis symptoms in the studied group is favorable with Vladimir's study.

In a study by Mamdoh et al., a comparison between the users of Propolis mouthwash group and the chlorhexidine mouthwash group showed a significant decrease in the severity of mucositis based on the WHO criteria in the Propolis group ($p < 0.05$). In this study, Propolis' anti-inflammatory effect is dependent on the presence of flavonoids, which prevents the development of inflammation of the mucosa. This study indicated that, Propolis, as an anti-inflammatory agent, stimulates the immune system by enhancing phagocytic activity and cellular immunity, and promotes the effects of healing on epithelial tissues. Since Propolis contains components such as zinc and iron, it also plays an important role in the synthesis of collagen. A number of anti-inflammatory agents, such as flavonoids, have been found in Propolis, which have been shown to suppress the synthesis of prostaglandins and leukotrienes by macrophages, thereby contributing to their anti-inflammatory activity (2). The findings of this study are in line with the results of this study.

The results of the study by Blury et al., on the prophylactic and treatment effect of Propolis mouthwash on oral mucositis caused by radiotherapy showed that the difference in oral mucositis based on NIC-CTC criteria between the Propolis mouthwash using group and placebo using group was significant after intervention ($p < 0.05$), and in this regard, it is consistent with the results of this study.

In Blury study in all follow up stages (4 stages), the severity of mucositis in the Propolis group was significantly less than that in the placebo group, while in the present study, this difference was significant in the second and third follow up sessions ($p < 0.05$). In Blury study, as in the current study, there was no statistically significant difference in the distribution of sexes as well as the type of tumor and radiotherapy between the Propolis group and the placebo group ($p > 0.05$) (24, 25).

The results of the study by Akhavan and his colleagues about the effect of Propolis mouthwash on oral mucositis caused by chemotherapy in patients with head and neck cancer were also consistent with the results of this study.

In Akhavan study, the difference of mucositis severity based on WHO criteria was not significant between the Propolis group and the placebo on the third day of treatment (the first session of the follow up) ($p > 0.05$), but on the seventh day of treatment (the second follow up session), the difference in mucositis severity between the two groups was significant ($p < 0.05$) (24).

Also, in Akhavan Study, the severity of mucositis before and after treatment was statistically significant in the placebo group and was consistent with the present study, and this is due to the self-healing nature of oral mucositis. In the Propolis group, the difference in the severity of mucositis was significant before and after the intervention. In addition, the average mucositis severity was lower in all follow up sessions than in the placebo group, and this data can be indicative of the effect of Propolis on reducing the symptoms of oral mucositis (25).

In preclinical researches, Propolis was used on oral mucositis from radiotherapy and chemotherapy. Suemaru et al showed that the use of Propolis 1% and 3% in oral mucositis caused by 5-Fluorouracil chemotherapy in mice did not have a positive effect, however, Matlab Nejad and his colleagues showed that an increasing dose of Iranian Propolis could reduce the severity of oral mucositis caused by radiotherapy in rats.

In this study, patients consumed two oral tablets of 50 mg daily or, in other words, 100 mg oral propolis per day, and this dose reduced the symptoms of mucositis in the intervention group compared to the control group. These contradictory results probably reflect differences in the design and principles of the research, but this contradiction can also be due to the different origins of Propolis used in various investigations, because the biological activity of Propolis is derived from the active compounds that make up the substance and amount of those compounds is also dependent on the region where Propolis derives from.

The results of the study by Tomazevic et al. showed that the Propolis group did not significantly decrease the severity of oral mucositis in children under chemotherapy compared to the control group. The chemical analysis of Propolis used in the study demonstrated the presence of flavonoids and phenolic compounds as anti-inflammatory and antimicrobial compounds, although the difference between the intervention and control groups was not significant**.** One of the reasons for not being consistent with this study is that this can be attributed to the age range of patients participating in the project. In that study, the mean age of patients in the intervention group was 6 years and in the control group was 9 years, while in the present study, the mean age of the patients in the intervention group was 47 years and in the control group was 53 years (1).

Because young cancer patients with a higher rate of division than older patients are more susceptible to chemotherapy mucositis, the high severity of mucositis in this study can be attributed to the young age of patients.

However, due to the study limitations, they recommended more clinical research to confirm or reject the positive effects of Propolis on oral mucositis due to chemotherapy or radiotherapy (1 and 28).

## CONCLUSION

This study showed that the use of Systemic Propolis tablet could significantly reduce the incidence and severity of oral chemotherapy mucositis in patients with colon cancer.

Therefore, prescription of oral Propolis along with chemotherapy without having a counter effect, improves oral health in patients and reduces the potential side effects of oral mucositis, including oral ulcers and eating disabilities, and improves the quality of life of patients undergoing chemotherapy.

**Conflict of interest**

No conflict of interest was declared by the authors.

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