

# Evaluation the effectiveness of oral gel containing pomegranate peel extract in treatment of periodontitis

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ABSTRACT

**Background and Aim:** The goal of this project is to introduce an oral gel of plant origin for the treatment of gingivitis and periodontitis that is thought to have significant therapeutic effects while not having the side effects of common chemical agents. Due to no toxic and systemic side effects and on the other hand, given the antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, and astringent components of this product, it is assumed to be useful in clinical studies.

**Materials and Methods:** The study was triple blinded. The study population consisted of 32 patients (n=32) with moderate to severe periodontitis. The study included both men and women between the ages of 22 years-60 years for three months. Initially, two teeth in two different quadrants with deep pockets were considered in each patient. Each tooth and gels that has to be injected around teeth, were randomly selected. At the beginning, plaque index, gingival index, clinical attachment loss, pocket depth, bleeding index were measured and recorded. All patients treated with scaling and root planning, then one periodontal pocket of each patient was injected with pomegranate gel and another periodontal pocket was injected with placebo. The syringe was 1 ml and 27 gauge, then Coe-pack placed on both teeth. The trial interval was one and three months. After one and three months of the first session, variables were evaluated again.

**Results:** There was no statistically significant difference in plaque index, gingival index, clinical attachment loss, pocket depth and bleeding index at baseline between pomegranate gel and placebo. There was a statistically significant reduction in all mentioned variables one and three months after the beginning of the study in the tooth containing pomegranate gel ( $p < 0.001$ ). There was a significant reduction in plaque index, gingival index, clinical attachment loss, pocket depth and bleeding index in tooth containing pomegranate between the beginning of the study with one and three months follow-up ( $p < 0.001$ ). There was a significant reduction in plaque index, gingival index, clinical attachment loss, pocket depth and bleeding index in tooth containing placebo between the beginning of the study with one and three months follow-up ( $p < 0.001$ ).

**Conclusion:** The results of this study show that gel containing pomegranate peel extract can have good therapeutic effects on plaque index, gingival index, clinical attachment loss, pocket depth and bleeding index.

**Keywords:** gingivitis, periodontitis, clinical attachment loss, scaling and root planing, punica granatum

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## INTRODUCTION

A person's quality of life and his physical and mental condition in today's society depend highly on his oral and dental health. Also, studies have proven the association between many chronic and systemic diseases, including cardiovascular diseases, etc., and poor health conditions of the oral cavity [1]. Gingivitis and periodontitis are the most common types of gum disease. Gingivitis is only specific to the gums and does not invade the supporting tissues of the tooth (periodontal ligament, cementum, and alveolar bone) [1]. Gingivitis can turn into periodontitis if it is not treated and progresses [2]. Inflammatory mechanisms are also involved in the occurrence of periodontitis in addition to bacteria [3]. The worldwide prevalence of periodontal diseases is 20%-5% in the adult population. Periodontitis is the second most common oral health problem. It affects 10%-15% of the world's population. The most severe forms of periodontal disease are significantly found in adults aged 35 years-44 years with a prevalence of 19% [4]. Chronic periodontitis negatively affects people's beauty, chewing, and speaking [5]. The treatment of periodontitis is a crucial issue that includes several stages depending on the severity of the gum disease. The disease disappears in the initial stages of scaling and root planing [6]. The treatment includes curettage or gum surgery in more advanced stages.

Antibiotics, mouthwash, and antimicrobial toothpaste are mostly prescribed after the treatment of scaling and gum surgery [7]. Plaque on the teeth contains bacteria. Thus, taking antibiotics reduces the amount of plaque in the mouth [7]. These drugs may have side effects [8]. Plants are a rich source of active and effective compounds with countless therapeutic properties and minimal side and unwanted effects [9]. The use of medicinal plants to treat various diseases has been developed in recent years. Much scientific attention has been paid to herbal products to control oral and dental diseases. Studies have proven that some plants help to maintain the overall health of the mouth, in addition to protecting the teeth and gums. The pomegranate plant with the scientific name *Punica granatum L.* is an ancient plant and the most abundant genus of the *Punicaceae* family. Pomegranate is native to North India and Iran. It has been taken to all the Mediterranean areas and cultivated [10]. Various uses have been reported for it in Indian and Greek medicine. It has been used as an anti-parasitic agent, blood purifier, treatment of mouth sores, and digestive tract ulcers. It is also extensively applied in the Middle East, Iran, and India to treat diabetes [11].

The present study aims to present an oral gel with a completely natural and herbal origin that has significant therapeutic impacts. Also, it does not have the side effects of common chemical treatments. The current chemical drugs available in the market failed to help much in the treatment of periodontitis. Due to the limited side effects and the absence of toxic and systemic side effects and considering the antibacterial, antifungal, antiviral, anti-inflammatory, antioxidant, and astringent effects of this product, it is assumed that this herbal product can be used in the study. It clinically has significant therapeutic effects. This gel can be recommended in phase 3 (treatment) for the treatment of periodontitis instead of similar external substances if its effect is proven. The present study aims to investigate the effects of herbal gel obtained from the pomegranate peel and introduce it as a product in the treatment of periodontitis. If favorable clinical results are obtained, dentists can prescribe it by being sure of its efficiency, and finally, its domestic production will be supported.

## MATERIAL AND METHOD

The present study was conducted using an interventional method in the form of parallel assignment, controlled clinical trial, and triple-blind. The statistical population of the study included patients with moderate to severe chronic periodontitis. The patients who were referred to Kermanshah Dental Faculty were included in the study after being examined, confirming that they met the necessary criteria to participate in the study, and completing and signing the consent form. The results of previous studies were used to calculate the sample size. In the study by Sastravaha et al., the standard deviation of the PD variable in the SPT alone and apt<sup>+</sup> med groups was  $S_1=0.93$  and  $S_2=1.04$ , respectively, with the means  $X_1=6.21$  and  $X_2=6.93$ , respectively [12]. The minimum sample size was estimated to be 32 people considering  $\alpha=0.05$ , 90% test power, and  $\beta=-1$ . The optimal pharmaceutical form was prepared after evaluating and choosing the appropriate formulation by pharmaceutical colleagues. After packaging, it was used to conduct a clinical study. The efficacy and safety of the drug were evaluated in clinical studies. The study was conducted as a triple-blind (patient, interventionist, and examiner of results). The patients underwent initial examination and were selected based on the criteria of moderate to severe chronic periodontitis. The studied population included 32 patients ( $n=32$ ) with moderate to severe periodontitis. This survey included both male and female patients in the age range between 22 years and 60 years for three months.

The inclusion/exclusion criteria of the study are as follows: patients who did not receive any other periodontal treatment during the study other than the screening performed by the project executor, no history of hypersensitivity reactions, not consuming tobacco and alcohol, not receiving antibiotics and any type of medicine that affects periodontal conditions, not having systemic diseases that affect periodontal conditions (such as kidney, liver, or rheumatic diseases), non-pregnant or non-lactating women, and not receiving any orthodontic treatment. The patients were asked to sign the consent form after a detailed study. Also, the patients were encouraged to refrain from performing dental treatment on the studied teeth and their adjacent teeth during the study and postpone the treatment until the completion of the study.

First, the numbers of eligible teeth for the study were written on

paper in different quadrants and placed in one pocket (example: 13, 36, 45, etc.), and in another pocket, the codes A and B were written on the paper, which was the encrypted codes of the gel tubes by the drug manufacturer. Tubes containing drugs named A and B were coded by the drug manufacturer and provided to the project executor. Only the drug manufacturer was aware of the pomegranate gel or placebo content of each A and B tube until the end of the study. Since the patients had chronic periodontitis at moderate to severe degrees, the treatment plan included scaling, complete oral health education, and the use of a gel containing pomegranate and a placebo. Thus, the patients were asked to take a sheet from the teeth pocket and select the sheet from the tube coding pocket of the drugs. The selected tooth information and the injectable gel were entered into the checklist. Then, in the periodontal pocket of that tooth, the same selected gel was injected after the scaling and polishing treatment. Again, the patients were asked to select another tooth from the pocket in the same order, if the second chosen tooth is from the same quadrant as the first tooth. This sheet was discarded and the patients were asked to select another sheet to ensure that the second tooth was different from the quadrant of the first tooth. After recording the information and scaling and polishing, the gel that was not selected by the patient in the first step was injected into the periodontal pocket of the second tooth.

The checklist included selected tooth number and injectable gel code and study variables, plaque index, gingival index, clinical attachment loss, pocket depth, and bleeding index. The injection was done with a 27-gauge 1 ml syringe around the tooth. Then, a coe-pack was placed on both areas and the patients were asked to observe their oral health during the study. However, they were asked to avoid using dental floss in the studied area and using mouthwash. After one week, the patients were called to remove the dressing and evaluate the gum condition. The health education was given to them again. The test period was one month and three months after the start of the study. After one and three months from the initial session, the patients were called on. Based on the routine treatment plan for patients with periodontitis, the studied variables were re-measured in the follow-up sessions. Then, the results were analyzed using statistical software and relevant tests.

The data were collected by clinical observation and the Williams probe was used to fill out the checklist. The goals of the study were fully explained to the subjects who entered the study. After obtaining written consent from them by the project executor, information before the treatment 1 month and 3 months after the first session was entered into the checklist. The data of the study were analyzed in two sections: descriptive statistics and inferential statistics. In the descriptive statistics section, central tendency and dispersion criteria were reported along with the table. In the inferential statistics section, the normality of the data was checked using the kolmogorov-smirnov test. To compare two drugs, the paired samples T-test and Wilcoxon test were used. For follow-up comparisons, friedman and repeated measures tests were used. For pairwise comparisons, posthoc tests with significance levels adjusted by Bonferroni correction were used. Given the rank nature of PI, GI, and BI variables, non-parametric tests were used to analyze these variables. SPSS-24.0 software was used for data analysis. The significance level in this study was considered at 0.05. The project started after obtaining permission from the Ethics Council of Kermanshah University of Medical Sciences.

The written consent form was read and signed by the patients after providing a sufficient explanation. Then, the patients entered the study.

## RESULTS

A total of 32 people participated in the present study. Among them, 13 (40.6%) were male and 19 (59.4%) were female. The mean age of the participants was  $41.38 \pm 10.57$ . There was no statistically significant difference between drugs A and B regarding PI at the beginning of the study ( $p=0.627$ ). There was a statistically significant difference between drugs A and B

regarding PI one month after the start of the study ( $p<0.001$ ) so the mean of this variable was lower in drug A than in drug B. There was a statistically significant difference between drugs A and B regarding PI three months after the start of the study ( $p<0.001$ ) so the mean of this variable was lower in drug A than in drug B. There was a statistically significant difference between the follow-up times regarding PI in drug A ( $p<0.001$ ), so the mean of this variable in one and three months of follow-up was lower than at the beginning of the study. There was a statistically significant difference between follow-up times regarding PI in drug B ( $p<0.001$ ) so the mean of this variable in one and three months of follow-up was lower than at the beginning of the study (Table 1).

**Tab. 1.** Descriptive statistics of PI and its comparison between two treatments over time

	Treatment								p-value <sup>†</sup>
	A				B				
	Med	IQR	Mean	SD	Med	IQR	Mean	SD	
Baseline	2.00 <sup>b</sup>	1	1.66	0.83	2.00 <sup>b</sup>	1	1.72	0.85	0.627
1MO F/U	1.00 <sup>a</sup>	0.5	0.31	0.59	1.00 <sup>a</sup>	1	0.91	0.69	<0.001
3MO F/U	1.00 <sup>a</sup>	0	0.13	0.34	1.00 <sup>a</sup>	1	0.78	0.66	<0.001
p-value <sup>‡</sup>	<0.001				s<0.001				

Med: Median, IQR: Interquartile Range, SD: Standard Deviation

<sup>†</sup> Wilcoxon Signed Ranks Test

<sup>‡</sup> Friedman test, followed by Post-hoc of Friedman test. In each column, medians with the same superscript letter were not significantly different.

There was no statistically significant difference between drugs A and B regarding CAL at the beginning of the study ( $p=0.203$ ). There was a statistically significant difference between drugs A and B regarding CAL one month after the start of the study ( $p<0.001$ ), so the mean of this variable was lower in drug A than in drug B. There was a statistically significant difference between drugs A and B regarding CAL three months after the start of the study ( $p<0.001$ ), so the mean of this variable was lower in drug

A than in drug B. There was a statistically significant difference between the follow-up times regarding the mean CAL in drug A ( $p<0.001$ ), so the mean of this variable in three months of follow-up was lower than at the beginning of the study and one month of follow-up. There was a statistically significant difference between the follow-up times regarding CAL in drug B ( $p<0.001$ ), so the mean of this variable in 1 month and 3 month follow-ups was lower than at the beginning of the study (Table 2).

**Tab. 2.** Descriptive statistics of CAL and its comparison between two treatments over time

	Treatment				p-value <sup>†</sup>
	A		B		
	Mean	SD	Mean	SD	
Baseline	4.19 <sup>c</sup>	1.4	4.53 <sup>b</sup>	1.48	0.203
1MO F/U	1.78 <sup>b</sup>	1.52	3.44 <sup>a</sup>	1.66	<0.001
3MO F/U	1.59 <sup>a</sup>	1.36	3.28 <sup>a</sup>	1.59	<0.001
p-value <sup>‡</sup>	<0.001		<0.001		

SD: Standard Deviation

<sup>†</sup> Paired Samples T-Test

<sup>‡</sup> Repeated Measures test, followed by Post-hoc test with Bonferroni adjustment. In each column, means with the same superscript letter were not significantly different.

There was no statistically significant difference between drugs A and B regarding GI at the beginning of the study ( $p=0.499$ ). There was a statistically significant difference between drugs A and B regarding GI one month after the start of the study ( $p<0.001$ ), so the mean of this variable was lower in drug A than in drug B. There was a statistically significant difference between drugs A and B regarding GI three months after the start of the study ( $p<0.001$ ), so the mean of this variable was lower in drug A than in drug B. There was a statistically significant difference between follow-up times regarding GI in drug A ( $p<0.001$ ) so the mean of this variable in one- and three-month follow-up was lower than at the beginning of the study. There was a statistically significant difference between the follow-up times regarding GI in drug B ( $p<0.001$ ) so the mean of this variable in the three-month follow-up was lower than at the beginning of the study (Table 3).

and B regarding PD at the beginning of the study ( $p=0.209$ ). There was a statistically significant difference between drugs A and B regarding PD one month after the start of the study ( $p<0.001$ ), so the mean of this variable was lower in drug A than in drug B. There was a statistically significant difference between drugs A and B regarding PD three months after the start of the study ( $p<0.001$ ), so the mean of this variable was lower in drug A than in drug B. There was a statistically significant difference between the follow-up times regarding the mean of PD in drug A ( $p<0.001$ ), so the mean of this variable in three months of follow-up was lower than at the beginning of the study and one-month follow-up. There was a statistically significant difference between the follow-up times regarding PD in drug B ( $p<0.001$ ) so the mean of this variable in one- and three-month follow-up was lower than at the beginning of the study (Table 4).

There was no statistically significant difference between drugs A

**Tab. 3.** Descriptive statistics of GI and its comparison between two treatments over time

	Treatment								p-value <sup>†</sup>
	A				B				
	Med	IQR	Mean	SD	Med	IQR	Mean	SD	
<b>Baseline</b>	1.00 <sup>b</sup>	1.5	1.31	1	1.00 <sup>b</sup>	1	1.22	1.97	0.499
<b>1MO F/U</b>	0.00 <sup>a</sup>	0	0.16	0.37	1.00 <sup>ab</sup>	1	0.72	0.58	<0.001
<b>3MO F/U</b>	0.00 <sup>a</sup>	0	0	0	1.00 <sup>a</sup>	1	0.69	0.59	<0.001
<b>P-value<sup>‡</sup></b>	<0.001				<0.001				

Med:Median, IQR: interquartile range, SD:Standard Deviation

<sup>†</sup> Wilcoxon Signed Ranks Test

<sup>‡</sup> Friedman test, followed by Post-hoc of Friedman test. In each column, medians with the same superscript letter were not significantly different.

**Tab. 4.** Descriptive statistics of PD and its comparison between two treatments over time

	Treatment				p-value <sup>†</sup>
	A		B		
	Mean	SD	Mean	SD	
<b>Baseline</b>	3.84 <sup>c</sup>	1.48	3.53 <sup>b</sup>	1.39	0.209
<b>1MO F/U</b>	1.38 <sup>b</sup>	1.04	2.38 <sup>a</sup>	0.98	<0.001
<b>3MO F/U</b>	1.06 <sup>a</sup>	0.84	2.22 <sup>a</sup>	0.01	<0.001
<b>p-value<sup>‡</sup></b>	<0.001		<0.001		

SD: Standard Deviation

<sup>†</sup> Paired Samples T-Test

<sup>‡</sup> Repeated Measures test, followed by Post-hoc test with Bonferroni adjustment. In each column, means with the same superscript letter were not significantly different.

There was no statistically significant difference between drugs A and B regarding BI at the beginning of the study (p=0.740). There was a statistically significant difference between drugs A and B regarding BI one month after the start of the (p<0.001), so the mean of this variable was lower in drug A than in drug B. There was a statistically significant difference between drugs A and B regarding BI three months after the start of the study (p<0.001), so the mean of this variable was lower in drug A than in drug B. There

was a statistically significant difference between the follow-up times regarding BI in drug A (p<0.001) so the mean of this variable in 1 month and 3 month follow-up was lower than at the beginning of the study. There was a statistically significant difference between the follow-up times regarding BI in drug B (p<0.001) so the mean of this variable in 1 month and 3 month follow-up was lower than at the beginning of the study (Table 5).

**Tab. 5.** Descriptive statistics of BI and its comparison between two treatments over time

	Treatment								p-value <sup>†</sup>
	A				B				
	Med	IQR	Mean	SD	Med	IQR	Mean	SD	
<b>Baseline</b>	2.00 <sup>b</sup>	1.5	2.38	1.13	2.00 <sup>b</sup>	1	2.34	1.04	0.74
<b>1MO F/U</b>	1.00 <sup>a</sup>	1	0.84	0.68	2.00 <sup>a</sup>	1	1.75	0.8	<0.001
<b>3MO F/U</b>	0.00 <sup>a</sup>	1	0.44	0.5	2.00 <sup>a</sup>	1	1.72	0.81	<0.001
<b>p-value<sup>‡</sup></b>	<0.001				<0.001				

Med: Median, IQR: Interquartile Range, SD: Standard Deviation

<sup>†</sup> Wilcoxon Signed Ranks Test

<sup>‡</sup> Friedman test, followed by Post-hoc of Friedman test. In each column, medians with the same superscript letter were not significantly different.

## DISCUSSION

Periodontitis in males is more prevalent than in females, indicating the possible role of gender in the pathogenesis of the disease [13]. However, the ratio of females in the conducted study (59.4%) was higher than males (40.6%). The basic age groups related to periodontal health are 15 years-19 years, 35 years-44 years, and 65 years-74 years [14]. The patients in this study were in the age range of 22 years-60 years. At the end of the study and after data collection and statistical analysis by the statistician, the producer of study gels was asked to announce the pomegranate gel and placebo coded as A and B. The results of investigating the effect of pomegranate gel A compared to placebo B on the study variables include plaque index, gingival index, clinical attachment

loss, pocket depth, and bleeding index (For ease of understanding the results, group A teeth mean teeth treated with scaling and pomegranate gel and group B teeth means the teeth treated with scaling and placebo).

There was no significant difference between the two teeth selected by the patient at the beginning of the study, indicating the homogeneity of the condition of the two teeth in each patient. This study showed that the mean plaque index in the teeth of group A (0.13) had a significant decrease compared to the teeth of group B (0.78). A significant decrease in the mean plaque index occurred in the teeth of group A since the beginning of the study compared to 1 months and 3 months after the study. The reduction in the mean plaque index three months after the start of the study (0.13) was more than one month after the start of the study (0.31) in

the teeth of Group A, but this decrease was not significant. The mean plaque index in the teeth of group B decreased significantly over time from the beginning of the study compared to 1 months and 3 months after the beginning of the study. The mean plaque index 3 decreased significantly three months after the start of the study (0.78) than one month after the start of the study (0.91) in the teeth of group B, but this reduction was not significant. Results also showed that scaling alone will improve plaque index over time, but it is less effective than scaling with pomegranate gel. The mean gingival index showed no significant difference between the two teeth selected by the patient at the start of the study, indicating the homogeneity of the condition of the two teeth in each patient. This study revealed that the mean gingival index in group A teeth (0.00) decreased significantly compared to group B teeth (0.69).

A significant decrease was found in the mean gingival index in the teeth of group A at the start of the study compared to 1 months and 3 months after the start of the study. The mean gingival index decreased significantly three months after the start of the study (0.00) compared to one month after the start of the study (0.16) in the teeth of group A. However, this decrease was not significant. A significant decrease in the mean gingival index was found over time in the teeth of group B at the start of the study compared to 1 months and 3 months after the start of the study. The mean gingival index decreased significantly 3 months after the start of the study (0.69) compared to 1 month after the start of the study (0.72) in the teeth of group B. However, this decrease was not significant. This indicates that scaling alone will improve the gingival index over time, but it is less effective than scaling with pomegranate gel.

The mean bleeding index did not have a significant difference between the two teeth selected by the patient at the start of the study, indicating the homogeneity of the condition of the two teeth in each patient. This study revealed that the mean bleeding index in group A teeth (0.44) decreased significantly compared to group B teeth (1.72). A significant decrease in the bleeding index in the teeth of group A was found at the start of the study compared to 1 months and 3 months after the start of the study. The mean bleeding index decreased more three months after the start of the study (0.44) than one month after the start of the study (0.84) in group A teeth. However, this decrease was not significant. The mean bleeding index decreased significantly in group B teeth at the start of the study compared to 1 months and 3 months after the start of the study. The mean bleeding index showed a greater decrease 3 months after the start of the study (1.72) than 1 month after the start of the study (1.75) in group B teeth. However, this reduction is not significant. The results also showed that scaling alone over time causes an improvement in the bleeding index compared to scaling, but it is less effective than scaling combined with pomegranate gel.

No significant difference was found between the two teeth selected by the patient regarding the mean depth of the pocket at the start of the study, indicating the homogeneity of the condition of the two teeth in each patient. This study showed that the mean pocket depth in group A teeth (1.06) decreased significantly compared to group B teeth (2.22). A significant reduction was found in the depth of the pocket in the teeth of group A at the start of the study compared to 1 months and 3 months after the start of the study. The mean pocket depth 3 months after the start of the study (1.06) decreased significantly compared to 1 months after the

start of the study (1.38) in group A teeth. The mean depth of the pocket in the teeth of group B at the start of the study decreased significantly compared to 1 months and 3 months after the start of the study. The mean pocket depth decreased more than 3 months after the start of the study (2.22) compared to 1 month after the start of the study (2.38) in group B teeth. However, this reduction was not significant. The results revealed that scaling alone will improve pocket depth over time, but it is less effective than scaling combined with pomegranate gel.

The mean Clinical Attachment Loss (CAL) was not significantly different between the two teeth selected by the patient at the start of the study, indicating the homogeneity of the condition of the two teeth in each patient. This study showed that the mean Clinical Attachment Loss (CAL) in group A teeth (1.59) decreased significantly compared to group B teeth (3.28). A significant decrease was found in the mean Clinical Attachment Loss (CAL) in the teeth of group A at the start of the study compared to 1 months and 3 months after the start of the study. The mean Clinical Attachment Loss (CAL) decreased significantly three months after the start of the study (1.59) compared to 1 months after the start of the study (1.78) in group A teeth. The mean Clinical Attachment Loss (CAL) decreased significantly in the teeth of group B at the start of the study compared to 1 and 3 months after the start of the study. The mean Clinical Attachment Loss (CAL) decreased more than 3 months after the start of the study (3.28) and 1 month after the start of the study (3.44) in group B teeth. However, this decrease was not significant. It indicates that scaling alone will improve Clinical Attachment Loss (CAL) over time, but it is less effective than scaling with pomegranate gel.

In this study, the plaque index, bleeding index, and gingival index did not change significantly 1 months and 3 months after the start of the study in both group A and group B teeth, indicating that these variables are more affected by the oral health of the patients. Also, when patients visit for longer periods, their motivation to control oral health at home is reduced and it can affect these variables. Thus, it is recommended to examine these variables in shorter periods. In this study, pocket depth and clinical attachment loss variables showed significant differences between the start of the study and 1 months and 3 months after the start of the study and between 1 months and 3 months after the start of the study. This indicates that these variables are mostly affected over time and improvement in the periodontal attachment level and pocket depth occurs over time. It is consistent with the results of our study. None of the patients required periodontal surgery 3 months after the start of the study. In other words, the patients with Clinical Attachment Loss (CAL) of 3 mm or more were included in the study, and after scaling treatment in both the pomegranate gel-containing teeth and placebo gel, the depth of the pocket decreased to the patients did not need additional treatment such as surgery.

Sastravaha et al. conducted a study entitled "Periodontal adjuvant therapy with extracts of *Centella Asiatica* and *Punica granatum*." In the mentioned study, 20 patients with pocket depth of 5 mm-8 mm participated [15]. The reduction in pocket depth and improvement of CAL in this study are consistent with the results of our study, while other variables provided conflicting results. The criteria for selecting patients with chronic periodontitis in the mentioned study are patients with a pocket depth of 5 mm-8 mm, while the criteria for selecting patients in our study were patients with a CAL of 3 mm or more. Additionally, this study used



*Centella asiatica* along with pomegranate, and it is inconsistent with our study in some of the variables despite the appropriate and long duration of the study. It can justify the existing discrepancy. Salgado et al. conducted a study entitled "Anti-plaque and anti-gingivitis effects of a gel containing pomegranate extract". This double-blind study was conducted on 23 participants who were randomly divided into two control and intervention groups and received placebo gel and pomegranate gel, respectively [16]. The results of this study were inconsistent with those of our study. The reason for this discrepancy in the results is related to differences in the method of conducting the study. In our study, the gel was injected into the periodontal pocket.

Grover et al. investigated the effect of subgingival gel containing 10% *Emblica officinalis* as an adjunctive treatment for Scaling and Root Planing (SRP) in the treatment of chronic periodontitis" [17]. The results of this study regarding pocket depth and CAL showed that pocket depth was improved only in pockets of 5 mm and above although a different drug was used. It was consistent with our study. The studied plant has the same properties as the pomegranate plant. Thus, they are comparable in this respect. Also, in the mentioned study, like our study, the gel was placed subgingivally. However, the depth of the primary pocket of the teeth was not considered in the mentioned study, and any tooth that had a CAL above 3 mm was considered eligible for the study and the depth of the pocket of this tooth may be different (example: a tooth with a pocket depth of 6 mm has a CAL of 3 mm and another tooth with a pocket depth of 1 mm has a CAL of 3 mm, PPD=5 mm-6 mm, PPD  $\geq$  7 mm, and CAL  $\geq$  6 mm). However, in our study, a significant improvement in pocket depth occurred in all dental areas with different pocket depths from 1 mm to 7 mm.

Hrishi et al. investigated the effect of adjunctive use of green tea toothpaste in patients with periodontitis [18]. The results of the mentioned study in the basic variables of the study, including GI, PI, PD, and CAL, are consistent with those of our study. Although this study had a shorter investigation period (4 weeks) than our study, and the method of taking medicine was different from our study (toothpaste instead of injecting gel directly) and used toothpaste containing green tea, which is similar to pomegranate due to its antioxidant and phenolic properties, its satisfactory results are not different from our study. Rahimabadi et al. investigated the mouthwash (*Punica granatum* var *pleniflora*) to control the gums of diabetic patients [19]. This study investigated the variables relatively similar to the variables investigated in our study. Only the gingival index showed a significant improvement and was in line with our study. However, the results of other variables were inconsistent with the results of our study. Some primary differences between this study and our study are the method of conducting the study and the inclusion and exclusion criteria. In our study, patients with systemic diseases including diabetes were excluded from the study and the patients participating in our study were suffering from periodontitis. However, in this study, the patients suffered from gingivitis. Kiani et al. investigated the effect of pomegranate seed extract mouthwash on dental plaque and gingivitis. A total of 104 patients with gingivitis participated in this study [20]. This study only investigated the plaque index

and gingival index. The result of the improvement of the gingival index compared to the placebo was significant and consistent with our study. Regarding the plaque index, it is inconsistent with the result of our study. This is due to the difference in the method of conducting the study and other periodontal criteria that were not investigated.

Abullais et al. investigated the effectiveness of irrigation with different antimicrobial drugs on periodontal health in patients treated with chronic periodontitis. This study investigated the effect of subgingival washing with waterpick with Herbal Extract (HE) in comparison with 0.2% Chlorhexidine (CHX) on periodontal health [21]. The results of this study regarding plaque index are consistent with those of our study and other variables are different from our study. In addition to the difference in the methods of implementation, this study used a different drug than our study. It uses pomegranate, black pepper, and copper sulfate, which can provide results different from what pomegranate alone can do. Somu et al. investigated the effectiveness of herbal extract gel in the treatment of gingivitis [22]. In their study, the patients suffered from gingivitis, while the patients in our study suffered from periodontitis. Only the plaque index results were consistent with our study. In other variables, conflicting results were obtained, which may be attributed to the methods of conducting the study and the length of the study.

Megha et al. compared chlorhexidine gel and subgingival herbal gel in the treatment of chronic periodontitis. In this study, herbal gel contained pomegranate extract, Spanish cherry (*Mimusops elengi* (Bakul), and *Acacia Arabica* peel. All the study variables in the group of Scaling and Root Planing (SRP) with chlorhexidine and Scaling Root Planing (SRP) with herbal gel had a significant improvement compared to the control group [23]. It is consistent with the results of our study. However, in this study, the variables of the treatment group of Scaling and Root Planing (SRP) and herbal gel and Scaling and Root Planing (SRP) with chlorhexidine were not compared to see if the herbal gel was superior to chlorhexidine or not. Also, in this study, the herbal gel in addition to pomegranate contained two other plants. Masani et al. investigated the effect of a gel containing *Quercus brantii* (Iranian oak) and *Coriandrum sativum* as an adjunctive treatment for Scaling and Root Planing (SRP) in patients with moderate chronic periodontitis. *Quercus brantii* and *Coriandrum sativum* both have antioxidant, anti-inflammatory, and antibacterial properties and are similar to pomegranate in this respect [24]. No significant difference was found between the control and intervention groups in any of the variables. Contradictory results were obtained although the selected drug had properties similar to the properties of the drug used in our study, the periods of the study were similar to our study, and the method of transferring the drug to the teeth pockets was almost similar [24].

## CONCLUSION

The results of this study indicate that the gel containing pomegranate peel extract can have good therapeutic impacts on plaque index, gingival index, gum attachment level, pocket depth, and bleeding index.

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