



A Comparative Experimental Study of Healing Effect of Different Oral Wound Dressings for Oral Ulcers

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ABSTRACT

Objectives: Wound dressings protect the wound and accelerate the healing of ulcers. This study evaluated the role of distinct oral dressings in the wound healing of experimentally produced traumatic oral ulcers.

Materials and Methods: The study included 45 male Sprague-Dawley rats, which were randomly divided into three groups: Group 1, Group 2 and control group. Two different wound dressings were applied: hyaluronic acid (Group 1) and a wound dressing composed of a combination of bioactive materials (Group 2). Tissue samples were taken in the 3rd, 7th, 14th days and evaluated histopathologically. The Kruskal–Wallis test was utilized for analyzing numerical data across groups, followed by post-hoc testing to compare differences across groups were analyzed through the Chi-square test. The Chi-square test was explored for categorical data.

Results: Both wound dressings positively influenced the healing process compared with the control group. The hyaluronic acid–based dressing (Group 1) was associated with reduced ulceration scores and lower edema levels during the healing period. In contrast, the bioactive film dressing (Group 2) showed a more pronounced effect on early granulation tissue formation, particularly on day 3. Both treatment groups exhibited increased migration of polymorphonuclear leukocytes and mononuclear cells to the ulcer site during the early inflammatory phase.

Conclusions: Both wound coverings positively affected the wound healing process by regulating distinct phases of healing.

Keywords: Dental biomaterials, oral medicine, wound care

Farklı Oral Yara Örtülerinin Oral Ülserlerin İyileşmesi Üzerine Etkisinin Karşılaştırmalı Deneysel İncelenmesi

Araştırma Makalesi

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ÖZ

Amaç: Yara örtüleri, yarayı koruyarak ülserlerin iyileşmesini hızlandırır. Bu çalışma, deneysel olarak oluşturulan travmatik oral ülserlerin iyileşme süreci üzerine iki farklı oral yara örtüsünün etkisini değerlendirmek ve karşılaştırmak amacıyla tasarlanmıştır.

Gereç ve Yöntemler: Toplam 45 erkek Sprague-Dawley sıçandan oluşan çalışma üç gruba ayrılmıştır: kontrol, Grup 1 ve Grup 2. İki farklı yara örtüsü uygulanmıştır: hyaluronik asit (Grup 1) ve biyoaktif materyallerden oluşan bir kombinasyon (Grup 2). Doku örnekleri 3, 7 ve 14. günlerde alınarak histopatolojik olarak değerlendirilmiştir. Gruplar arasındaki sayısal değişkenlerin karşılaştırılmasında Kruskal-Wallis testi, ikili karşılaştırmalarda ise post-hoc testler kullanılmıştır. Kategorik veriler için Ki-kare testi uygulanmıştır.

Bulgular: Kontrol grubuna kıyasla her iki yara örtüsü de iyileşme sürecini olumlu yönde etkilemiştir. Hyaluronik asit bazlı yara örtüsü (Grup 1), iyileşme süreci boyunca daha düşük ülserasyon skorları ve daha düşük ödem düzeyleri ile ilişkili bulunmuştur. Buna karşılık, biyoaktif film yara örtüsü (Grup 2), özellikle 3. günde olmak üzere erken dönemde granülasyon dokusu oluşumu üzerinde daha belirgin bir etki göstermiştir. Her iki tedavi grubunda da erken inflamatuvar fazda polimorfonükleer lökositler ve mononükleer hücrelerin ülser bölgesine göçünde artış izlenmiştir.

Sonuçlar: Her iki yara örtüsü de iyileşmenin farklı evrelerini düzenleyerek oral ülserlerin iyileşme sürecini olumlu yönde etkilemiştir.

Anahtar Kelimeler: Dental biyomateryaller, oral tıp, yara bakımı

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Introduction

Oral ulcers are defined as lesions that involve the loss of tissue.¹ The process of wound healing is intricate and

involves multiple stages, and any deviation in the final stage can result in excessive wound healing or chronic

scarring.² Wound dressings are medical materials that allow the wound to be protected from external factors and stimulate the ulcer healing by activating the cellular response.^{3,4} Hyaluronic acid (HA) is responsible for stimulating cytokine production and thus angiogenesis by macrophages.^{5,6} Hydrogel films produced from cross-linked HA are considered as polymeric drug carrier biomaterials.⁶ Hydroxyethyl cellulose adheres to mucous membranes and has a matrix effect that enables the active ingredient to release very slowly and gradually over the course of up to 24 hours.⁷ Carboxylic acids react with the hydroxyl groups of cellulose, increasing the water resistance of the materials.⁸ α -tocopherol enables neutrophils and macrophages to gain antioxidant properties.⁹ Parabens have wide antimicrobial effect spectrum, sensitivity reduction, stability in a wide pH range.¹⁰

Although various topical agents have been proposed for the management of oral ulcers, comparative evidence regarding their biological effects on different phases of oral wound healing remains limited. Most previous studies have focused on clinical outcomes or the evaluation of single biomaterials, with few providing detailed histopathological comparisons under standardized experimental conditions.¹¹⁻¹³

Hyaluronic acid plays an important role in wound healing by modulating inflammation and supporting tissue regeneration. Bioactive wound dressings combine multiple components that protect the wound surface and promote early healing responses.^{5,14}

This study seeks to address this gap by comparing the effects of two distinct bioactive wound dressings—one containing HA and the another formulation composed of hydroxyethyl cellulose, α -tocopherol, methyl paraben, and polycarboxylic acid, tested in relation to traumatic oral ulcer healing. However, the differential effects of these materials on oral ulcer healing have not been sufficiently clarified. The findings of this research have the potential to inform clinical practices in wound care and improve patient outcomes. Therefore, this study aimed to comparatively evaluate the healing effects of a hyaluronic acid-based wound dressing and a bioactive film dressing on experimentally induced palatal ulcers in rats using a phase-specific histopathological approach. The study focused on analyzing the inflammatory and regenerative processes associated with ulcer healing and aimed to provide histopathological insight into the potential of these wound dressings to improve healing outcomes, with possible implications for clinical treatment strategies.

Materials and Methods

Ethics Approval and Consent to Participate

This study was conducted in accordance with the principles of the Declaration of Helsinki (revised 2008). Ethical approval for the experimental procedures was obtained from the Hacettepe University Animal Experiments Local Ethics Committee, under approval number (2019/08-13). This study was also designed and reported in accordance with the ARRIVE guidelines to

ensure transparency and reproducibility in the use of animal models.

Animals

Forty-five healthy male white Sprague-Dawley rats (8-10 weeks, weighing 250 to 300 g) were utilized. All experiments were conducted in the Hacettepe University Laboratory Animal Research and Application Center. All procedures performed with experimental animals comply with ethical standards. They were housed in the Hacettepe University Experimental Animal Laboratory (Ankara, Türkiye) in standard laboratory conditions with free accessibility to soft food and drinking under veterinary supervision. They were kept individually in separate cages during their treatment.

A randomization procedure was applied to distribute the rats into 3 groups, comprising 2 intervention groups (Group 1, Group 2) and a control group. Fifteen animals for each group were included in the study at 80% power, 5% significance level. The distribution of study groups was according to product used. Experimental days were determined as the 3rd, 7th and 14th day. The experimental design and study workflow are summarized in Figure 1.

Surgical procedures

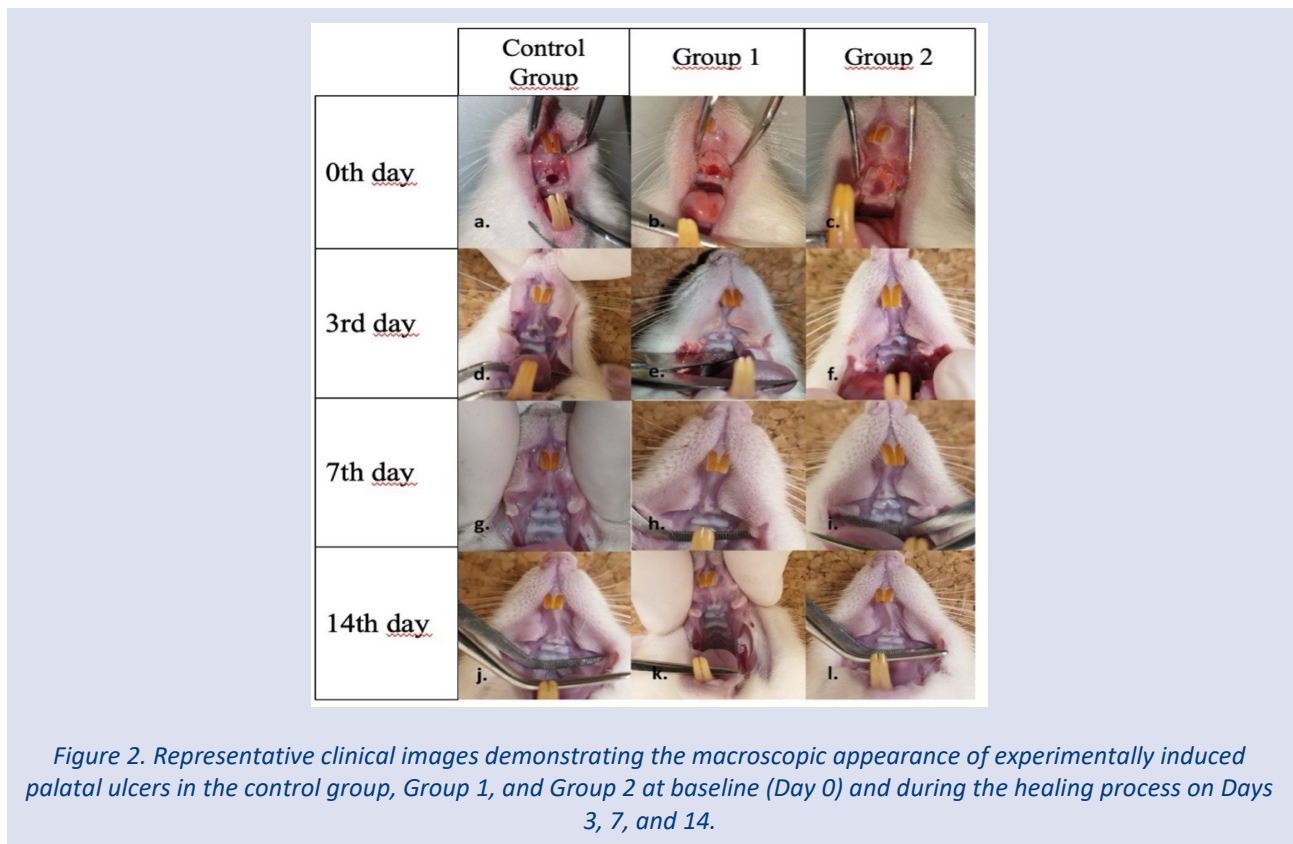
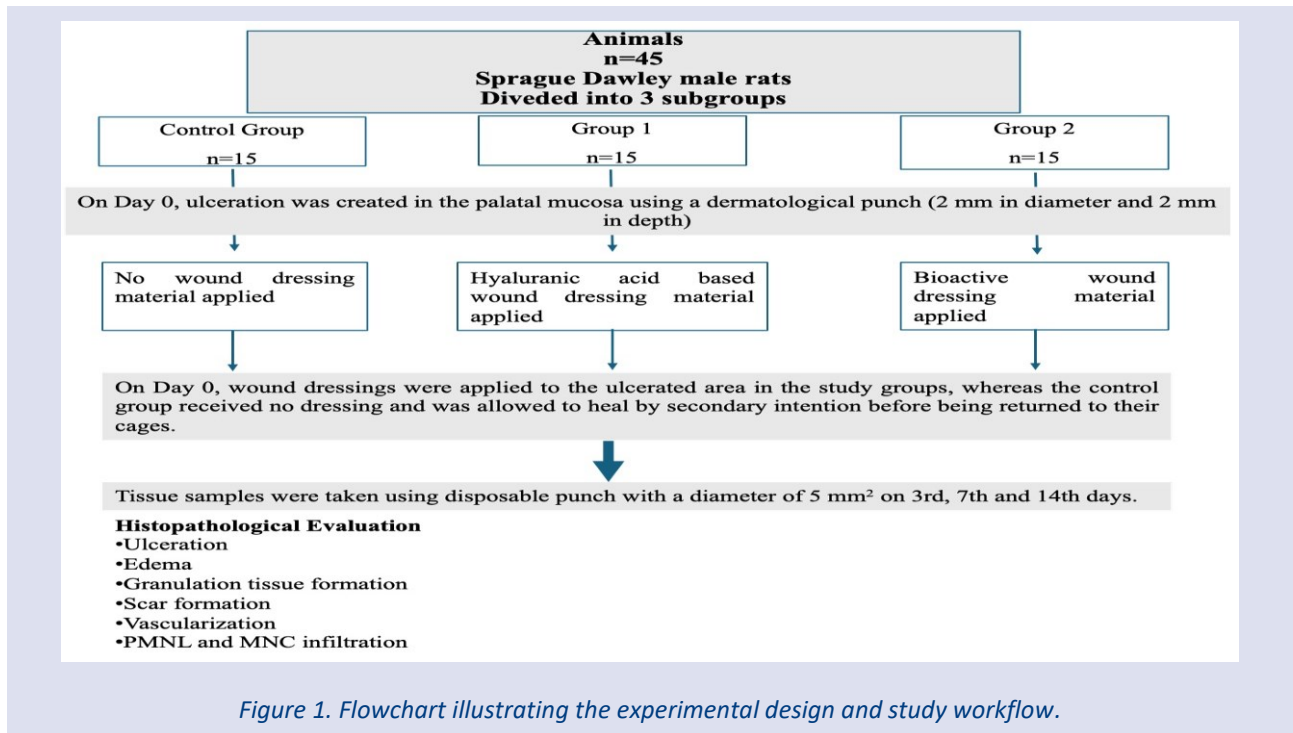
All rats were anesthetized with ketamine (Ketazol %10, Richter Pharma Ag, Wels, Austria) and Xylazine hydrochloride (Rompun %2, Bayer AG, Istanbul, Turkey) (90 mg/kg and 10 mg/kg body weight, respectively) on day 0. Subsequently, ulceration was created in the palatal mucosa using a dermatological punch (2 mm in diameter and 2 mm in depth), after which the epithelial covering was excised with a No. 15 scalpel blade. (Figure 2A, B, C).¹⁵⁻¹⁸

The surgical interventions were conducted by one operator in order to minimize differences among the ulcers. After the bleeding was controlled with sterile buffer, the oral ulcers in the control group received no material application and were allowed to undergo secondary healing. Different wound dressings were applied to each study group. Wound dressing containing HA (Aftamed® Oral gel – AktiFarma; Istanbul, Turkey) was applied topically in the amount to cover the wound surface to the oral ulcer in Group 1 (Figure 2B). The viscous nature of the HA gel provided a semi-adhesive effect that helped the gel to stay in contact with the wound. To further secure the gel, the rats were kept in their cages to minimize excessive movement that could potentially dislodge the gel. In Group 2, a thin film dressing (Ora-Aid® - TBM Co.; Gwangju, Republic of Korea) was applied to the oral ulcer in size of 3 x 3 mm² (Figure 2C), with its components enhancing mucosal adherence. All rats were placed back in their cages. The retention of the wound dressings on the palatal wounds was achieved through the inherent mucoadhesive properties of the materials during the immediate postoperative period, without the use of additional mechanical fixation, suturing, or protective retention techniques. The dressings remained in place throughout the recovery period until the animals regained

consciousness from anesthesia, which typically occurred within approximately 30–60 minutes under the ketamine/xylazine protocol.

Following recovery from anesthesia, the animals were allowed to resume routine oral conditions, including

normal feeding and oral function, without restriction. This approach was intentionally designed to simulate clinical intraoral conditions and to evaluate the effectiveness and retention of the wound dressings under physiological oral challenges.



Histopathological Processing and Analysis

For histopathological analysis, 5 rats randomly selected from each group were sacrificed with an

overdose of carbon dioxide on each experimental time. Tissue samples were taken using disposable punch with a diameter of 5 mm². All tissue samples were randomly

numbered. After fixed in 10% neutral buffered formalin for 24 to 48 hours the alcohol was passed through xylol series and blocked in paraffin. Sections of 4 micron thickness taken by microtome were stained with hematoxylin-eosin and evaluated blindly by a pathologist using various scores under light microscopy.

Parameters as the presence of ulceration, edema, granulation tissue formation, scar formation, vascularization were evaluated histopathologically for the control and study groups in all tissue samples. Histopathological evaluation was conducted through both qualitative observation and a scoring system previously defined in the literature.¹⁹ Scores, ranging from 0 to 4, were analyzed as ordinal categorical variables. Group comparisons were conducted using the Kruskal–Wallis test. New granulation tissue development was measured on the basis of minimal contraction in the ulceration sites. And the formation of new capillary buds in the ulcer site was measured. These parameters were examined in tissue samples on the experimental days. The number of rats in which each parameter as granulation tissue formation, vascularization, polymorph nuclear leukocytes (PMNL), and mononuclear cells (MNC) was observed, recorded, and presented in tables.

PMNL and MNC were also scored in 3 categories as mild, moderate, and severe for all specimens. At a high magnification (x 400), less than 5 cells are categorized as mild, 5 to 30 moderate, severe for more than 30. Histological sections were qualitatively scored using the method of Cavalcante et al.¹⁹

Statistical Analysis

Numerical data were expressed as median values with minimum and maximum ranges. Categorical variables were presented as frequencies and percentages. Intergroup comparisons of numerical variables were carried out using the Kruskal–Wallis test, followed by appropriate post-hoc analyses for pairwise evaluations. Associations between categorical variables were

examined using the Chi-square test, with the exact test applied where required. Effect sizes were reported alongside p-values to provide further context. For the Kruskal–Wallis test, eta-squared (η^2) values were interpreted as follows: <0.06, small effect; 0.06–0.14, moderate effect; >0.14, large effect. For Chi-square analyses, Cramer's V (CV) values were interpreted as <0.2, small effect; 0.2–0.6, moderate effect; and >0.6, large effect. Statistical analyses were conducted using IBM SPSS Statistics version 26 (IBM Corp., Armonk, NY, USA), and visualizations were produced in R (version 4.3.0; R Foundation for Statistical Computing, Vienna, Austria) with the “ggplot2” package. A p-value of <0.05 was considered statistically significant.

Results

The ulcer's macroscopic appearance demonstrated noticeable differences in wound healing over time between the study and control groups. The clinical appearance of the palatal ulcer area was evaluated prior to sacrifice on Days 0, 3, 7, and 14. At baseline (Day 0), comparable ulcerative lesions were observed in all groups immediately after ulcer creation (Figure 2A,2B, and 2C). On Day 3, the ulcer area remained clearly visible in all groups, with differences in surface characteristics and surrounding mucosal appearance (Figure 2D,2E, and 2F). By Day 7, a marked reduction in the ulcer area and improvement in mucosal integrity were observed across the groups, indicating ongoing healing (Figure 2G,2H, and 2I).

On Day 14, the ulcer area appeared substantially reduced in all groups, with near-complete mucosal recovery evident in representative images (Figure 2J,2K,2L). Histopathological findings showed variations in each evaluation parameter, including the presence of ulceration, edema, granulation tissue formation, polymorph nuclear leukocyte count and mononuclear cell count, vascularization (Figure 3).

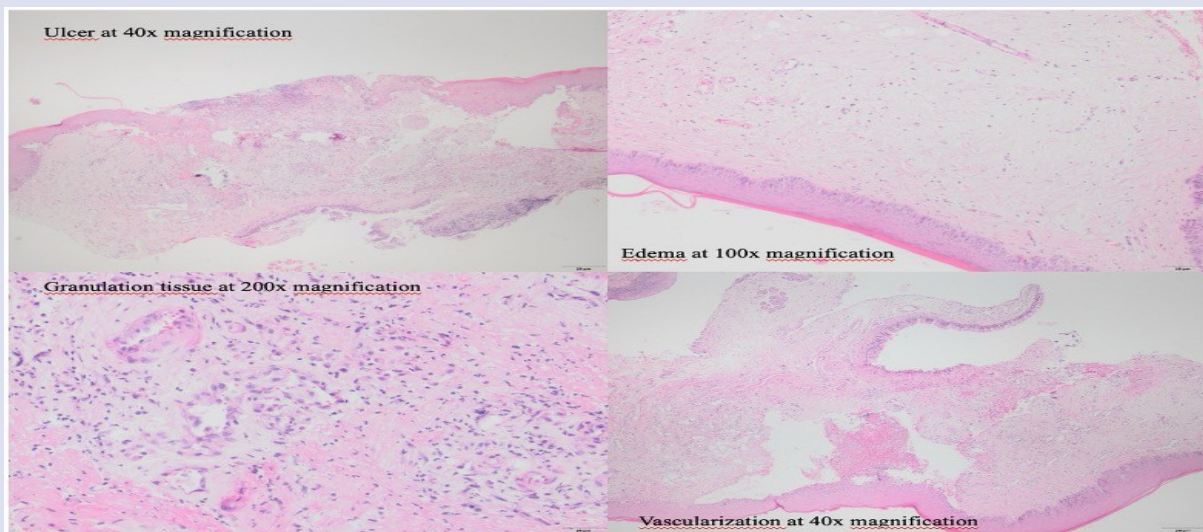


Figure 3. Histopathological evaluation of tissue samples.

Ulceration: The ulceration score was assessed histopathologically (Figure 4). As shown in Table 1, a statistically significant difference was found among the control (median [min; max]: 1 [0; 3]), Group-1 (median [min; max]: 1 [1; 1]), and Group-2 (median [min; max]: 3 [0; 4]) on the 3rd day.

However, no significant differences were observed between groups on the 7th and 14th days ($p < 0.05$; $\eta^2 = 0.39$ for 3rd day, $p > 0.05$ for 7th day, and $p > 0.05$ for 14th day). Group 2 had higher score values than the other

groups on the 3rd day. No significant differences were noted when comparing the 3rd, 7th, and 14th time points within the control group and Group-1 ($p > 0.05$, $p > 0.05$ respectively). A significant difference was found between the 3rd day and other days in Group 2 ($p = 0.007$; $\eta^2 = 0.67$). The score values on the 3rd day in Group 2 (median [min; max]: 3 [0; 4]) were significantly higher than those values on the 7th (median [min; max]: 1 [1; 1]) and 14th days (median [min; max]: 1 [1; 1]).

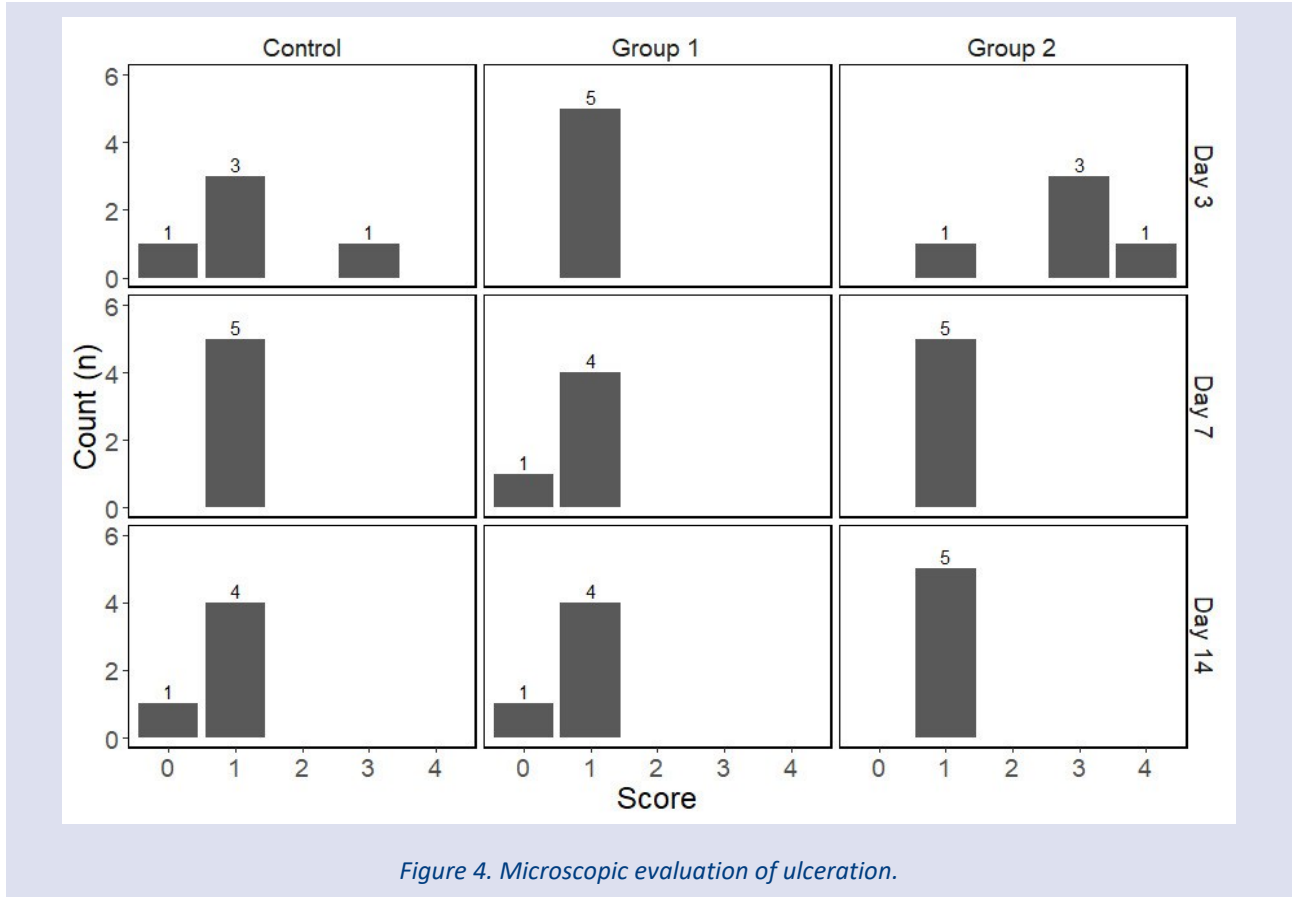


Figure 4. Microscopic evaluation of ulceration.

Table 1. Microscopic evaluation of ulceration

	Control group	Group-1	Group-2	p
Day 3	1 [0 - 3] ^a	1 [1 - 1] ^a	3 [1 - 4] ^{ba}	0.035*
Day 7	1 [1 - 1]	1 [0 - 1]	1 [1 - 1] ^B	0.368
Day 14	1 [0 - 1]	1 [0 - 1]	1 [1 - 1] ^B	0.584
p	0.731	0.584	0.007*	

The data are presented as median (minimum- maximum). Uppercase and lowercase letters indicate differences between days within Group-2 and experimental Groups within Day 3, respectively. Distinct letters represent statistically different between groups.

*Statistically significant at level $p < 0.05$ (Kruskal Wallis Test)

Granulation Tissue: Granulation tissue formation was observed (Figure 5), with a statistically significant difference across experimental days within Group-2 ($p = 0.001$; $CV = 0.7$). No significant differences were observed within the control group and Group-1 ($p > 0.05$; $CV = 0.39$ and $p > 0.05$; $CV = 0.5$, respectively; Table 2). Granulation tissue was absent in the control, Group-1, and Group-2 on the 7th and 14th days. On the 3rd day, granulation tissue was observed in 5 rats in Group-2, 3 rats in Group-1 and 2 rats in the control group. However, no significant

differences were found between the groups on the 3rd day ($p > 0.05$; $CV = 0.37$).

Vascularization: Vascularization was observed in all rats sacrificed on the 3rd day. The rate of vascularization varied in the samples taken on the 7th day and 14th day ($p > 0.05$; $CV = 0.47$ for the control group; $p > 0.05$; $CV = 0.41$ for Group 1; $p > 0.05$; $CV = 0.41$ for Group 2; Table 2).

Comparing the groups at each time point, no statistically significant differences were found in the presence of vascularization ($p > 0.05$ for all time points; Figure 5).

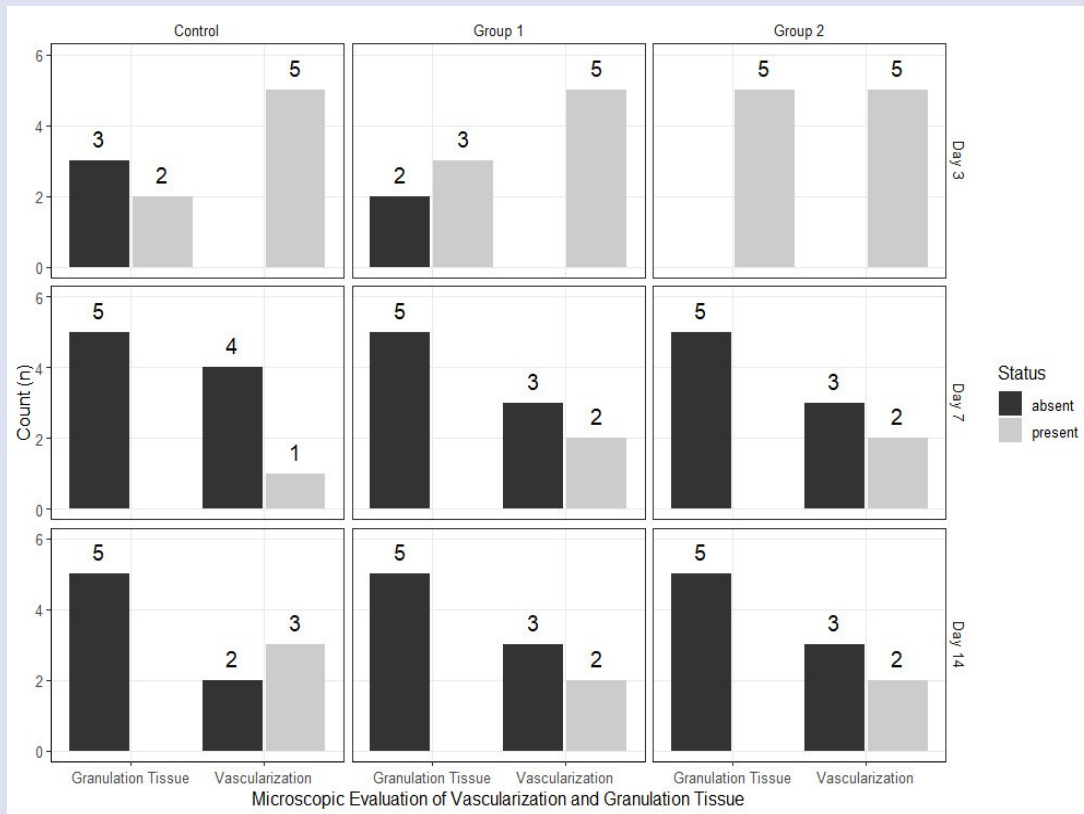


Figure 5. Microscopic evaluation of granulation tissue and vascularization.

Table 2. Microscopic evaluation of vascularization and granulation tissue

	Vascularization				Granulation tissue			
	Control	Group 1	Group 2	p	Control	Group 1	Group 2	p
Day 3	5 (100%)	5 (100%)	5 (100%)	NA	2 (40%)	3 (60%)	5 (100%)	0.251
Day 7	1 (25%)	2 (40%)	2 (40%)	>0.999	0 (0%)	0 (0%)	0 (0%)	NA
Day 14	3 (60%)	2 (40%)	2 (40%)	>0.999	0 (0%)	0 (0%)	0 (0%)	NA
p	0.066	0.201	0.201		0.286	0.066	0.001*	

The data are presented as frequency (percentage). NA: non-applicable

*Statistically significant at level $p < 0.05$ (Chi-Square Test)

Polymorphonuclear leukocyte (PMNL): The effects of wound dressing on PMNL cells migration to the wound area are shown in Figure 6. On the 3rd day, significant differences in cell migration were observed for control, Group-1, and Group-2 ($p < 0.05$; CV = 0.5, $p > 0.001$; CV = 0.6, $p < 0.001$; CV = 0.71, respectively; Table 3).

A mild presence of PMNL was found in all rats sacrificed on the 7th day and 14th day. When comparing the groups at each time point, no clinically or statistically significant differences were observed on the 3rd day ($p > 0.05$; CV = 0.38). The results on the 7th and 14th days were consistent across all groups (Figure 6).

Table 3: Microscopic evaluation of polymorphonuclear leukocyte

	Category	Control group	Group 1	Group 2	p
Day 3	Mild	2 (60%)	1 (20%)	0 (0%)	0.174
	Moderate	3 (60%)	2 (40%)	3 (60%)	
	Severe	0 (0%)	2 (40%)	2 (40%)	
Day 7	Mild	5 (100%)	5 (100%)	5 (100%)	NA
	Moderate	0 (0%)	0 (0%)	0 (0%)	
	Severe	0 (0%)	0 (0%)	0 (0%)	
Day 14	Mild	5 (100%)	5 (100%)	5 (100%)	NA
	Moderate	0 (0%)	0 (0%)	0 (0%)	
	Severe	0 (0%)	0 (0%)	0 (0%)	
	p	0.022*	0.004*	<0.001*	

The data are presented as frequency (percentage). NA: non-applicable

* Statistically significant at level $p < 0.05$ (Chi-Square Test)

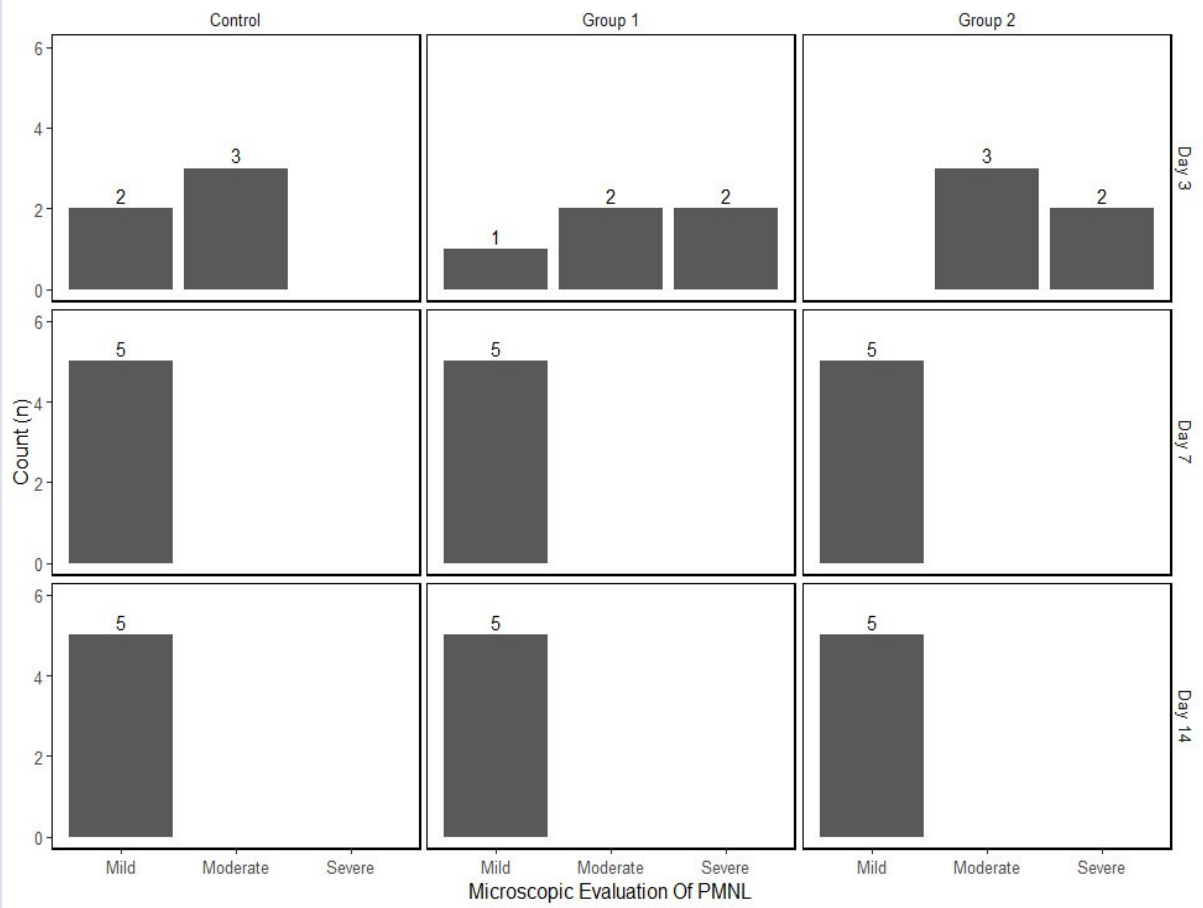


Figure 6. Microscopic evaluation of PMNL.

Mononuclear cell (MNC): The rates of MNC migration to ulcer site across days and groups are shown in Figure 7. A mild number of MNCs were primarily observed in the control group on the 3rd and 14th days. All rats exhibited moderate MNC presence on the 7th day ($p < 0.05$; CV = 0.53). No significant differences in MNC migration to the wound site were observed in Group-1 ($p > 0.05$; CV = 0.4);

however, the proportion of rats in the mild category increased over time ($p > 0.05$; CV = 0.52; Table 4).

When comparing the groups at each time point, a statistically significant difference was observed on the 7th day ($p < 0.05$; CV = 0.67). No significant differences were observed between the groups on the 3rd and 14th days, ($p > 0.05$; CV = 0.41 and $p > 0.05$; CV = 0.38; Figure 7).

Table 4. Microscopic evaluation of mononuclear cells

	Category	Control group	Group 1	Group 2	p
Day 3	Mild	4 (80%)	2 (40%)	1 (20%)	0.141
	Moderate	1 (20%)	3 (60%)	3 (60%)	
	Severe	0 (0%)	0 (0%)	1 (20%)	
Day 7	Mild	0 (0%)	4 (80%)	2 (40%)	0.021*
	Moderate	5 (100%)	1 (25%)	3 (60%)	
	Severe	0 (0%)	0 (0%)	0 (0%)	
Day 14	Mild	4 (80%)	5 (100%)	5 (100%)	0.368
	Moderate	1 (20%)	0 (0%)	0 (0%)	
	Severe	0 (0%)	0 (0%)	0 (0%)	
	p	0.014*	0.231	0.068	

The data are presented as frequency (percentage).

*Statistically significant at level $p < 0.05$ (Chi-Square Test)

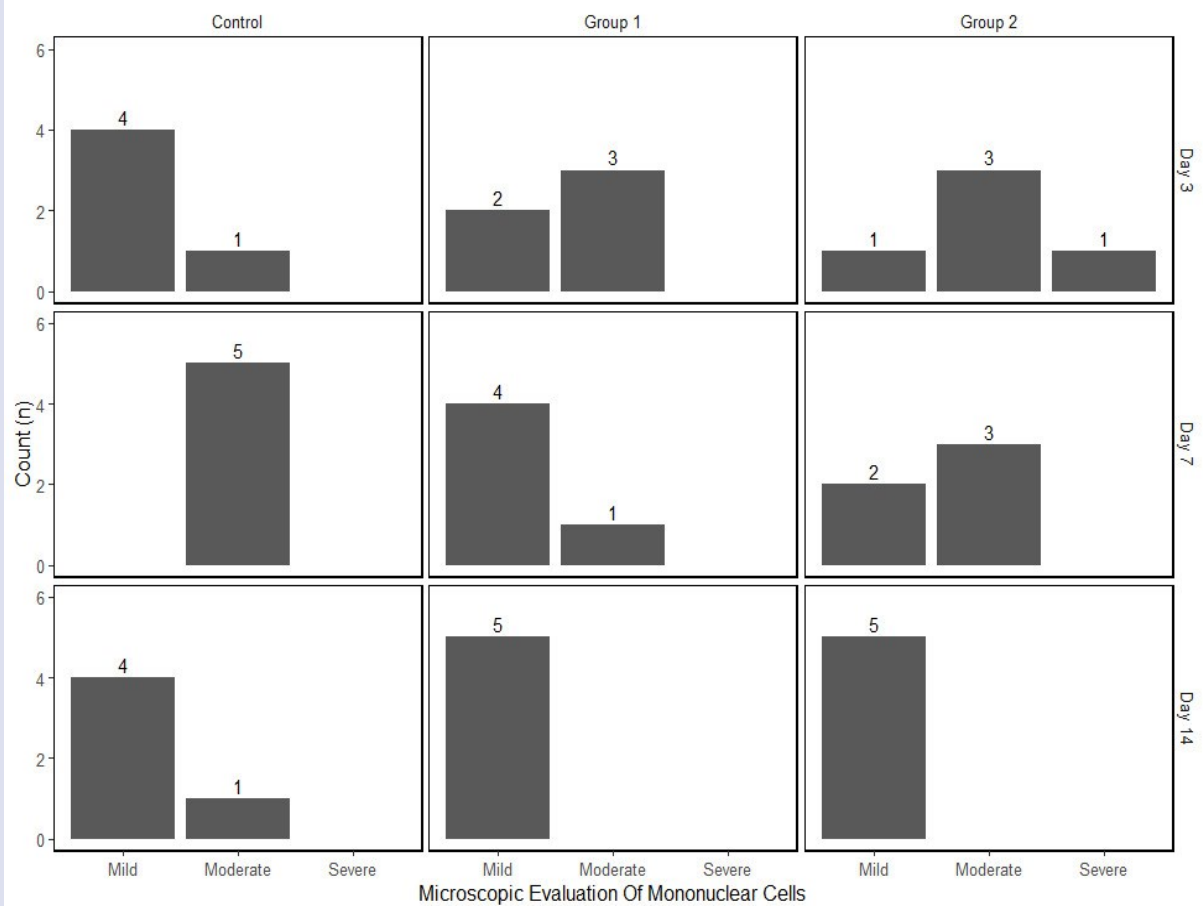


Figure 7. Microscopic evaluation of MNC.

Discussion

In roughly 5 to 25% of the general population, traumatic oral ulcers have a direct impact on the patients' quality of life and everyday activities.²⁰ The main purpose of healing in oral wounds is to reduce pain, continue function and comfort the patient.^{1,21} Among the purposes of wound dressings include providing physical protection and promoting healing.⁴ Wound dressing containing HA which stimulate endothelial cell proliferation, migration and angiogenesis, modulate inflammatory processes is one of the wound dressings widely reported in the literature.²²⁻²⁴ However, there is rare study in the literature about the effect of the second wound dressing used in this study. In a clinical study in which Bozkurt et al.²⁵ compared microbial adhesion and found that second wound dressing reduces biofilm formation. The effect of microbial control is the missing part of the current study. Min et al.²⁶ examined the effects of second wound dressing on wound healing clinically and found second wound dressing showed faster wound healing. Salih²⁷ and Taqi et al.²⁸ found that the second wound dressing used in this study showed less pain with protection of surgical area, reduced post-operative bleeding and promote healing of the socket. Similar to current study, Rodrigues et al.²⁹ showed that second wound dressing was more effective in healing clinically. Haykel and Lateef³⁰ reported that second wound dressing helped to prevent dry socket

occurrence and stabilized the blood clot. Akyildiz et al.³¹ found that HA showed the highest total ossification postoperatively. One of the shortcomings of this study is that it does not contain data on hard tissue healing. And also since this study is an experimental animal model, it has some limitations. The effects of two materials on healing in the oral ulcer model were examined, but the clinical parameters related to the patient could not be evaluated. An optimal wound healing agent reduces inflammation and stimulates cell proliferation to help regenerate damaged tissue.^{1,4} In the literature, wound healing processes have frequently been investigated using rat models.³² Many investigators have noted that the action of HA on oral ulcers is effective in wound healing.^{24,31} Hammad et al.²⁴ compared the effects of different wound dressings in a rat ulcer model histopathologically. Similar to this study, on the 7th and 14th days, there was a noticeable decrease in the ulcer area and an increase in epithelization when HA was used. Kang et al.³³ evaluated the second wound dressing in terms of epithelialization and proliferating cell number parameters. Similar to this study, the results showed improved wound closure and reconstruction in study group. These findings are corroborated by the current study's results as well as by other parameters that were looked at. In this study, a significant difference was observed between the control and study groups on the

3rd day, while it was found that the control group and Group 1 had similar effects in healing the ulcer tissue in the early period, while Group 2 was less effective.

Beyond the descriptive histopathological findings, the observed differences between the two wound dressings may be explained by their distinct biological mechanisms. Hyaluronic acid is a key component of the extracellular matrix and has been shown to regulate inflammatory cell activity, promote angiogenesis, and facilitate fibroblast migration and epithelial regeneration. Through these mechanisms, hyaluronic acid contributes to a more controlled inflammatory response, which may account for the reduced edema and more balanced healing pattern observed in Group 1.

In contrast, the bioactive film dressing evaluated in the present study incorporates multiple components with complementary biological roles. Hydroxyethyl cellulose provides a protective and mucoadhesive scaffold, while α -tocopherol exerts antioxidant effects that may enhance early cellular activity and inflammatory cell recruitment. This multimodal structure may explain the more pronounced granulation tissue formation and inflammatory cell migration observed during the early healing phase, particularly on day 3.

Unlike many previous studies that have primarily focused on clinical outcomes or single biomaterials, the present study offers a comparative, phase-specific histopathological evaluation of two oral wound dressings with different biological mechanisms. This approach allows a more detailed interpretation of the dynamic healing process and highlights the distinct contributions of each material at different stages of wound repair.

The histopathological findings of the present study may have important implications for clinical practice. The observed reduction in ulceration and edema associated with the hyaluronic acid-based dressing suggests its potential benefit in managing painful inflammatory phases of oral ulcers, where patient comfort and inflammation control are critical. Conversely, the enhanced early granulation tissue formation observed with the bioactive film dressing indicates a possible advantage in promoting early tissue repair and wound stabilization. These findings suggest that the selection of oral wound dressings in clinical practice may be optimized according to the predominant healing phase and therapeutic objective, rather than relying on a single universal approach.

A statistically significant difference was found among the Control, Group-1 and Group-2 on the 3rd day. ($p < 0.05$) It is concluded that the wound dressing used in Group 2 had less effect on healing the ulcer tissue in the early period, but the effect on healing on the 7th day did not differ significantly from the other wound dressing. The defect area is filled with granulation tissue, with capillary vascularization at the wound center and edges and underlying cellular proliferation. Closure of the defect occurs through wound contraction, which is driven by the activity of fibroblasts in the granulation tissue.³⁴ The histological findings obtained from this study are similar

to these informations. Following the formation of the ulcer, fresh bleeding findings and inflammatory cell infiltration are observed for both dressings. It was determined that the epithelial dehiscence surrounding the wound surface decreased over time with the formation of granulation tissue that started to form from the 3rd day. In this study, in which newly developed capillary vascularization in the lesion was evaluated, vascularization was observed in all rats in the early period, while vascularization was similarly decreased on the 7th and 14th days. When comparing the groups at each time point, although no statistically significant difference was found in the presence of vascularization ($p > 0.05$), granulation tissue formation was observed, with a statistically significant difference detected across experimental days within Group 2 ($p = 0.001$). On the 3rd day, granulation tissue was observed in 5 rats in Group 2, 3 rats in Group 1, and 2 rats in the control group. Similar to the current study, Şahin et al.³⁵ found that HA has increased the formation of granulation tissue on the 3rd day. Leukocytes come to the damaged area to remove substances that will impair healing, so the tissue repair can begin. Monocytes differentiate into specialized tissue macrophages to produce inflammatory and immunological mediators and regulate reactions that lead to chronic inflammation.^{11,34} In this study, it was seen that Group 2 is more effective than Group1 and the control group, respectively, in increasing the migration of PMNL and MNC to the wound area in 3rd day. On the 7th day, a decrease was observed in the number of MNC in the study groups, more prominently in Group 1, while a significant increase was observed in the control group. The results obtained on the 14th day do not show a significant difference between the groups. The number of PMNLs at the wound site on days 7 and 14 was similar for each group. The effects of wound dressing on PMNL cells migration to the wound area showed significant differences in cell migration were observed for control, Group-1, and Group-2 ($p = 0.022$; $p = 0.004$; $p < 0.001$, respectively). When comparing the groups regarding the effects of wound dressing on MNC cell migration to the wound area at each time point, a statistically significant difference was observed on the 7th day ($p < 0.05$). However, no significant differences were observed between the groups on the 3rd and 14th days ($p > 0.05$).

Several limitations of the present study should be acknowledged. First, although an experimental animal model allows standardized wound creation and controlled histopathological evaluation, the healing dynamics of rat palatal mucosa may not fully replicate those of human oral tissues. Second, the retention of the wound dressings was evaluated under physiological oral conditions without additional fixation. However, quantitative measurements of retention duration were not performed. In addition, the study focused primarily on histopathological outcomes, and functional parameters such as pain perception or feeding behavior were not assessed. These limitations should be considered when extrapolating the findings to clinical practice.

Conclusions

Topical application of wound dressings was effective in promoting oral ulcer healing. Both materials demonstrated favorable effects on the wound repair process by reducing inflammatory responses and supporting tissue regeneration in experimentally induced oral ulcers. These findings indicate that the evaluated wound dressings may represent safe and effective therapeutic options for the management of oral ulcers.

Future research should further investigate the effects of novel wound dressings on hard tissue healing and oral mucositis. In addition, studies conducted in larger animal models and clinical settings are warranted to validate the present findings under real-world intraoral conditions. Comparative investigations incorporating patient-centered outcomes, such as pain reduction, comfort, and functional recovery, as well as repeated application protocols and longer follow-up periods, may provide deeper insight into the long-term clinical relevance of these materials.

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Conflicts of Interest Statement

No conflicts of interest. This study was derived from the PhD/ speciality thesis of the first author.

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