Lauric Acid as a Topical Agent for Oral Wound Healing in Sprague-Dawley Rats

Christian Noel E. Paghubasan, DDM, Melanie Ruth M. Karganilla, DDM,
Marie Rossini Carmela T. Lachica, DDM, MScD and Florentino Kurt P. Lozano III, DDM, MScD

Department of Clinical Dental Health Sciences, College of Dentistry, University of the Philippines Manila

ABSTRACT

Background. Soft tissue wounds are common in the oral cavity and can be treated with various medicines. Several conventional treatments aid in wound healing; however, some are expensive and have side effects. Consequently, natural products and their components have been studied for their potential wound-healing properties. An example of this is coconut oil, which is often credited with various health benefits and contains lauric acid as its primary fatty acid component. Lauric acid has been shown to possess anti-inflammatory, antioxidant, and antibacterial properties; however, its effect on wound healing has yet to be explored.

Objective. The study aimed to determine the effect of lauric acid on the healing of experimentally induced soft tissue wounds on the buccal mucosa of Sprague-Dawley rats.

Methods. Forty-eight male Sprague-Dawley rats were randomly assigned to one of three main groups and subjected to a wounding procedure using a 4 mm diameter punch biopsy instrument, followed by daily application of a topical material. The vehicle control group (n = 16) received hydroxyethyl cellulose gel (HEC); the experimental group (n = 16) received lauric acid gel (LA); and the positive control group (n = 16) received 0.2% hyaluronic acid gel (HA). The three main groups were further divided into four subgroups and randomly assigned to an experimental time point (day 3, 7, 14, 21). Soft tissue wound healing at each time point was evaluated using the Healing Index (HI), by computing the Percentage Area Reduction (PAR), and through histological examination. Statistical analyses were performed using the Kruskal-Wallis test and post-hoc Dunn's test.

Results. HI scores within the three main groups and across different experimental time points showed a significant difference ($p<0.05$); however, the HI of subgroups assigned to the same experimental time point was not statistically different. PAR and HHS results showed no significant difference between the LA and HA groups.

Conclusion. Lauric acid promotes healing of soft tissue wounds on the buccal mucosa of Sprague-Dawley rats.

Keywords: lauric acid, wound healing, topical agents, coconut oil, buccal mucosa

eISSN 2094-9278 (Online)
Published: August 15, 2026
https://doi.org/10.47895/amp.v60i15.14036

Corresponding author: Christian Noel E. Paghubasan, DDM
Department of Clinical Dental Health Sciences
College of Dentistry
University of the Philippines Manila
Pedro Gil St. cor. Taft Ave., Ermita, Manila 1000, Philippines
Email: cepaghubasan@up.edu.ph
ORCiD: https://orcid.org/0009-0000-7218-0133

INTRODUCTION

Soft tissue wounds are relatively common in the oral cavity, leading to pain, discomfort, swelling, or infection.[1] These wounds can result from tooth brushing, chewing food, or even during dental treatment, and they may sometimes heal improperly.[2] When the oral mucosa is injured, the body responds immediately with bleeding and an inflammatory response, followed by healing that involves various cellular and molecular mechanisms.[3]

Healing of oral wounds may be influenced by factors such as saliva, oral bacteria, and mouth movement, and some of these wounds may experience delayed or impaired healing and do not respond adequately to conventional treatment,

posing a greater challenge for treatment and management.[4,5] Wounds in the oral mucosa can be treated with various topical medicines.[6] While several conventional treatments exist to aid in wound healing, some of these medications can be relatively expensive and may have reported side effects.[7] Currently, there is increasing interest in exploring natural compounds for their potential wound-healing properties.[8] One such example is coconut oil, with its lauric acid content often cited as a reason for its health benefits.[9] Many studies highlight the positive health benefits of using coconut oil; however, only a limited number of studies regarding the effects of lauric acid are available.

Lauric acid, which contributes to a significant portion of fatty acids in coconut oil (approximately 50%), has been reported to possess anti-inflammatory, antioxidant, and antibacterial properties.[3,10,11] However, its effect on the healing of soft tissue wounds in the oral cavity has not yet been studied. Therefore, this preliminary in vivo study aimed to determine if lauric acid affects the healing of soft tissue wounds on the buccal mucosa of Sprague-Dawley rats and potentially establish its value as an oral wound-healing medication.

MATERIALS AND METHODS

Lauric Acid Gel Preparation

Lauric acid in solid, white, crystalline form was procured from a GMP-certified and FDA-accredited local chemical supplier. Other chemicals and components of the topical formulation were locally available and purchased from a private chemical laboratory. The lauric acid gel was prepared in a GMP-certified chemical laboratory in Laguna using the fusion method, in which hydroxyethyl cellulose (HEC) was dissolved in a mixture of distilled water, glycerin, EDTA, sodium benzoate, and sorbitol. Lauric acid, comprising 10% of the formulation, and PEG-40 stearate were gradually added to the base and continuously stirred at 79-82 °C until homogeneous. The gel formulation was placed in a small, transparent, airtight glass container, allowed to set at room temperature, and stored away from direct sunlight. After 24 hours, a physicochemical evaluation of the semi-solid formulation was performed (Table 1).

Table 1. Physicochemical Evaluation of 10% Lauric Acid Gel

Parameter	Result(s)
Form	Semi-solid, gel
Color	White, off-white
Texture	Smooth, non-grainy
Appearance	No visible grains or lumps
Consistency	Smooth, homogeneous
pH	6.8-7.2

Relative viscosity was estimated by performing a spreadability test via a parallel plate method. Results showed a mean spread diameter (MSD) of 4.15 ± 0.05 cm, indicating a smaller spread or a slightly higher viscosity than the gel base (MSD = 4.75 ± 0.03 cm). A sterility test was also performed through direct inoculation of the material into the Fluid Thioglycollate medium (FTM). After the 14-day incubation period, turbidity was not observed in the culture medium, confirming the sterility of the prepared formulation.

A hydroxyethyl cellulose (HEC) gel base for the vehicle control group was prepared using components procured from a private chemical laboratory, while 0.2% hyaluronic acid (HA) gel (Gengigel®), serving as the positive control, was purchased from the official local dental distributor.

Animals

Based on an *a priori* sample size computation (effect size = 0.5124, power = 0.823, α = 0.05), the minimum required sample size was 4 animals per subgroup per experimental time point, corresponding to 16 animals per treatment group, with a total of 48 animals for the entire study.

Forty-eight (48) male Sprague-Dawley rats aged 8-10 weeks and weighing 150-200 g were obtained from a Bureau of Animal Industry-accredited facility. Prior to and following transport, the health status of all animals was verified by a licensed veterinarian based on a Body Conditioning Score (BCS)of 3 and the presence of intact buccal mucosa.[12,13] At the study site, the licensed veterinarian randomly selected the rats from the transport cage and placed them in groups of four, housing them in unlabeled polypropylene cages (92 in^2 floor area, 7 in height) with stainless steel wire covers and separate compartments for food and water. An autoclaved paper tube was provided in each cage for enrichment.[14] A cereal-based fixed formula (soy, wheat, corn) was provided daily at approximately 10% of body weight, and distilled water was given ad libitum. Conditions were maintained at 18–26 ± 2 °C, 40–60% humidity, under a 12:12 light-dark cycle.[15] All animals underwent a 7-day acclimatization period before experimentation.

Sampling

After the 7-day acclimatization period, systematic random sampling was conducted by one of the researchers to assign the animals to their groups and experimental time points. The home cages were randomly labeled with a number from 1 to 12, and an online number list randomizer was used to rearrange numbers 1 to 12. The first 4 numbers on the list were assigned to the vehicle control group, the next 4 numbers to the experimental group, and the last 4 numbers to the positive control group. To randomize the home cages further, the groups were rearranged from the lowest to the highest number and were finally assigned a letter-number code: A1 to A4 for the vehicle control group, B1 to B4 for the experimental group, and C1 to C4 for the positive control group. In addition, to easily identify an individual rat within

the group, a line was placed on its tail using a colored, non-toxic marker.

Treatment Groups

The animal groups were also assigned to specific experimental time points (Day 3, 7, 14, and 21). Animals in the A1, B1, and C1 groups were assigned for Day 3 and were scheduled for sacrifice three days later; Groups A2, B2, and C2 were set for Day 7, scheduled to be sacrificed 7 days after wounding. The A3, B3, and C3 groups were sacrificed 14 days after wounding, while the A4, B4, and C4 groups, designated for Day 21, were sacrificed 3 weeks following the wounding procedure.

Experimental Procedure

To ensure standardization, a single researcher performed anesthesia administration, wounding procedure, and topical material application. The researcher responsible for these procedures was blinded to the subgroups and treatment.

Wounding Procedure

Anesthesia was induced via intraperitoneal injection with a mixture of 25 mg Tiletamine and 25 mg Zolazepam (Zoletil® 50) at 20 mg/kg.[16] The mouth was opened and secured with sanitized elastic bands, exposing the right buccal mucosa. Disinfection with 5 mL of 0.12% Chlorhexidine Gluconate for 30 seconds, then a 6 x 6 mm area was marked with a surgical skin marker pen. A wound was created with a 4.0 mm diameter, 0.5 mm depth tissue punch to obtain a cylindrical tissue sample (Figure 1-A0, B0, C0), which was separated with a No. 15 blade.[17-19] The wound was allowed to bleed and was exposed to air and saliva for 2 minutes without intervention, then irrigated with 5 mL of 0.9% NSS, dampened, and compressed using a sterile gauze with firm pressure until the wound bed was clean and clearly visible. Wound dimensions were immediately measured and verified using a UNC-15 periodontal probe.

Application of Lauric Acid and Other Topical Materials

The control group received HEC gel base, the experimental group received lauric acid gel, and the positive control group received 0.2% hyaluronic acid. After drying the wound area with sterile gauze, a pea-sized amount (approximately 0.036 grams) of topical medicament was applied to each animal's wound to adequately cover the area.[20] After application, the animal was fasted for 30 minutes to maximize contact time, placed in a temporary cage over a heating pad for monitoring and recovery before being returned to its home cage where it was provided with the standard diet and water.

Daily Application of Topical Material

Visual examination of the soft tissue wound, measurement of the animal's weight, and observation of the animal's general condition were performed daily to monitor post-wounding recovery and before reapplication of the topical materials. The animals were sedated each day using an intraperitoneal injection of ketamine (40-100 mg/kg) combined with xylazine (5-10 mg/kg).[21] This procedure was repeated daily until the designated experimental time point was reached. Animals not scheduled for sacrifice on day 3, as well as those randomly selected to remain until the end of the experiment (day 21), received the anesthetic mixture for 21 days.

Animal Sacrifice and Tissue Sample Collection

Animals were sacrificed at designated time points via cervical dislocation. Buccal mucosa samples were collected using an 8 mm punch biopsy, fixed in 10% buffered formalin, embedded in paraffin, sectioned at 5 μm, and stained with hematoxylin and eosin (H&E).

Wound Healing Assessment

Two (2) independent examiners assessed soft tissue wound healing using three methods: the Healing Index (HI), Percentage Area Reduction (PAR), and Histologic Healing Score (HHS). Prior to the wound evaluation, the examiners underwent a calibration process through discussion and review of the clinical and histologic evaluation criteria to ensure consistent scoring and interpretation. The calibration included evaluation of photographs and representative histologic slides of unwounded buccal mucosa from the animals to standardize the interpretation of normal tissue architecture and wound healing features. To minimize observer bias, the examiners were blinded to the treatment groups and experimental time points during assessment. Evaluation of clinical photographs and microscopic slides for wound healing was performed using coded samples and images, which were decoded only by one of the researchers.

Clinical assessment of the soft tissue wound was performed at the experimental time points using the Healing Index developed by Landry, Turnbull, and Howley.[22] Each soft tissue wound was assessed using the following clinical parameters: tissue color, bleeding on palpation, granulation tissue, incision margin, and suppuration. Each parameter was rated on a scale from 1 to 5, with 1 indicating very poor healing and 5 denoting excellent healing.

Digital planimetry was also used to measure and calculate the total wound area in each animal.[23] Wound images were captured using a mirrorless digital camera with a 30 mm f/2.8 macro lens, mounted on a tripod to ensure consistent distance and angle relative to the right buccal mucosa. A UNC-15 periodontal probe served as a reference scale. Images were taken in triplicate, and the best-quality image was selected for evaluation. The wound margin was traced using the digital image of the wound using the Freehand Selections tool in ImageJ software. After tracing, the Measure option was selected to obtain values for the wound area (in mm^2). The measurement was repeated three times for each image to obtain an average value, which was subsequently

used to calculate the Percentage Area Reduction (PAR) for each animal. To calculate the PAR, the wound area at the designated experimental time point was subtracted from its measurement at day 0. The resulting value was then divided by the initial wound area and multiplied by 100 to express it as a percentage.

Histological evaluation was performed using a modified scoring method by Sultana et al., where the histological healing score (HHS) was derived by summing the scores from the four histological parameters of wound healing: the amount of granulation tissue and inflammatory infiltrates, and the orientation and arrangement of collagen fibers.[24] Total scores were categorized as good (9 – 12), fair (5 – 8), and poor (<5).

Statistical Analysis

Descriptive statistics were used to summarize the data. To determine whether lauric acid has an effect on soft tissue wound healing and to analyze the results of the wound healing assessment methods in all groups, the Kruskal-Wallis test was utilized. Due to the non-normal distribution of data, a non-parametric test was used for data analysis, followed by a post-hoc Dunn's Test. A *p*-value of less than 0.05 was considered statistically significant.

Ethical Considerations

The study was conducted with approval from the Institutional Animal Care and Use Committee, University of the Philippines Manila (Protocol No. 2024-007).

RESULTS

Reliability Tests

A Cohen's kappa (κ) analysis was performed to determine inter-reliability between the two examiners for each wound healing assessment method. The results showed strong agreement across all evaluation parameters (HI, κ = 0.925; PAR, κ = 0.955; HHS, κ = 0.911), confirming the reliability and accuracy of the data used. Additionally, the test statistics (HI = 6.450; PAR = 399; HHS = 10.7) and *p*-values (<0.001) suggested sufficient evidence to conclude that the level of agreement is statistically significant at the 0.05 level of significance.

Healing Index (HI)

Table 2 showed that all animals in the A1 subgroup had an HI score of 1, indicating very poor healing, whereas only one rat in each of the B1 (Rat 2) and C1 (Rat 1) subgroups received the same score. The subgroups randomly assigned to day 7 (A2, B2, and C2) achieved a majority score of 2, with an equal distribution among the three treatment groups. Furthermore, the B2 and C2 subgroups had the same number of animals with HI scores of 2, 3, and 4. The animals randomly selected for day 14 had HI scores of 4, while only one rat in the group received a score of 3 (Rat 2). In particular, all rats from the B3 and C3 subgroups received an HI score of 4, indicating very good wound healing. The majority of the HI scores received by the animals in subgroups A4, B4, and C4 were also 4. Additionally, two rats from the B4 (Rat 1 and Rat 3) and C4 (Rat 4) subgroups received the highest index (HI = 5).

Table 2. Summary of Healing Index (HI) Results and Kruskal-Wallis Test of Different Treatment Groups

Treatment Group	Sub-group	Healing Index								Test statistic (H)	*p*-value
		E1 Rat 1	E2 Rat 1	E1 Rat 2	E2 Rat 2	E1 Rat 3	E2 Rat 3	E1 Rat 4	E2 Rat 4		
HEC	A1	1	1	1	1	1	1	1	1	14.12	0.0027*
	A2	1	1	2	2	3	2	2	2		
	A3	4	4	3	3	4	4	4	4		
	A4	4	4	4	4	3	4	3	4		
LA	B1	2	2	2	1	2	2	1	1	12.18	0.0068*
	B2	3	3	2	2	4	4	2	2		
	B3	4	4	4	4	4	4	4	4		
	B4	5	5	4	4	5	5	4	4		
HA	C1	2	1	2	2	1	1	2	2	11.85	0.0079*
	C2	2	2	2	2	3	3	4	4		
	C3	4	4	4	4	4	4	4	4		
	C4	4	4	4	4	4	4	5	5		

**Statistically significant at p <0.05*

Table 3. Dunn's Test *(with Bonferroni Correction)* for Multiple Pairwise Comparisons on HI Subgroups

Sub-groups	HI	
	Test statistic (Z)	*p*-value
A1 vs. B1	-1.177	0.239
A1 vs. C1	-1.177	0.239
B1 vs. C1	0.000	1.000
A2 vs. B2	-1.471	0.141
A2 vs. C2	-1.471	0.141
B2 vs. C2	0.00	1.000
A3 vs. B3	-0.588	0.556
A3 vs. C3	-0.588	0.556
B3 vs. C3	0.00	1.000
A4 vs. B4	-1.177	0.239
A4 vs. C4	-0.588	0.556
B4 vs. C4	0.588	0.556

The Kruskal-Wallis test showed a significant difference among the HI scores of the treatment groups; however, it also revealed that the HI scores of the subgroups assigned to the same experimental time point were not significantly different. A post-hoc Dunn's test analysis (Table 3) further confirmed that there were no differences in HI scores among the specified subgroups.

Percentage Area Reduction (PAR)

The A1 subgroup (Figure 1-A1) achieved a mean PAR of 37.24% ± 13.31 (Table 4), the lowest in both its treatment group and among all subgroups. The B1 (Figure 1-B1) and C1 (Figure 1-C1) subgroups also recorded the lowest mean PAR scores in their respective treatment groups. Although these scores remain higher than those of A1, statistical analysis using the Kruskal-Wallis test showed no significant differences in mean PAR among these subgroups.

The subgroups A2, B2, and C2 (Figures 1A2, B2, and C2) exhibited a higher mean PAR than those assigned to the previous experimental time point. At this point, the subgroups had a mean PAR of more than 50%, indicating that the soft tissue wound had already decreased to more than half of its original size. Statistical analysis revealed that the mean PAR between subgroups B2 and C2 was not significant (g = 0.35, 95% CI [-0.59, 1.28]); however, there were significant differences between subgroups A2 and B2 (g = 2.80, 95% CI [1.32, 4.28]), and A2 and C2 (g = 1.48, 95% CI [0.29, 2.67]).

By day 14, the soft tissue wounds of subgroup C3 (Figure 1C3) were completely closed, while those in B3 remained slightly open (Figure 1-B3). In contrast, the wound margins of subgroup A3 were still visible (Figure 1-A3), resulting in a mean PAR of 79.62% ± 3.76. Dunn's test (Table 5) indicated that subgroups A3 and B3 (g = 6.22, 95% CI [3.92, 8.52]), as well as A3 and C3 (g = 7.15, 95% CI [4.54, 9.77]), were statistically different from each other, while B3 and C3 were similar.

Daily treatment on subgroups B4 (Figure 1B4) and C4 (Figure 1C4) produced complete wound closure on day 21, while the soft tissue wound in subgroup A4 (Figure 1-A4) remained traceable and had a mean PAR of 88.45%. Based on post hoc Dunn's test (Table 5), the treatment effect in subgroups A4 and B4, as well as A4 and C4, was significantly different (g = 6.55, 95% CI [4.14, 8.96]), whereas the difference between B4 and C4 was not significant.

Histologic Healing Score (HHS)

All animals in the A1 subgroup predominantly exhibited a mean score of 4.13 ± 0.35, indicating poor healing (Table 6). At this experimental time point, the animals in both the lauric acid and hyaluronic acid-treated groups had the same score (HHS = 6), indicating fair wound healing. However, statistical analysis showed no difference among the scores of the three subgroups.

On day 7, the HHS of subgroup A2 indicated fair wound healing, whereas the wounds in the experimental and positive control groups had already demonstrated good healing. A representative slide (Figure 2B) shows an ulcerated area with sparse collagen, an elevated epithelial area, and granulation tissue. A noticeable fibrinous area can be noted adjacent to the ulceration. In contrast, the soft tissue wound treated with LA exhibited early signs of remodeling and collagen deposition (Figure 2C). Table 7 also showed that the mean scores of subgroups A2 and C2 differed statistically (g = 5.92, 95% CI [3.72, 8.12]), whereas those of subgroups B2 and C2 did not.

The B3 and C3 subgroups both showed good wound healing, as evidenced by scant granulation tissue and fewer

Table 4. Summary of Percentage Area Reduction (PAR) Results and Kruskal-Wallis Test of Different Treatment Groups

Treatment Group	Sub-group	PAR		
		Mean ± SD	Test statistic (H)	*p*-value
HEC	A1	37.24% ± 13.31	12.18	0.0068*
	A2	61.22% ± 6.83		
	A3	79.62% ± 3.76		
	A4	88.45% ± 1.67		
LA	B1	65.20% ± 18.61	10.96	0.0119*
	B2	76.06% ± 2.11		
	B3	98.44% ± 1.21		
	B4	100.00% ± 0.00		
HA	C1	63.23% ± 11.07	10.40	0.0155*
	C2	80.39% ± 16.50		
	C3	100.00% ± 0.00		
	C4	100.00% ± 0.00		

**Statistically significant at p <0.05*

Table 5. Dunn's Test *(with Bonferroni Correction)* for Multiple Pairwise Comparisons on PAR Subgroups

Subgroups	PAR	
	Test statistic (Z)	*p*-value
A1 vs. B1	-1.667	0.096
A1 vs. C1	-1.863	0.062
B1 vs. C1	-0.196	0.844
A2 vs. B2	-2.942	0.003*
A2 vs. C2	-2.353	0.019*
B2 vs. C2	-0.588	0.556
A3 vs. B3	-2.353	0.019*
A3 vs. C3	-2.942	0.003*
B3 vs. C3	-1.177	0.239
A4 vs. B4	-2.353	0.019*
A4 vs. C4	-2.353	0.019*
B4 vs. C4	0.000	1.000

**Statistically significant at p <0.05*

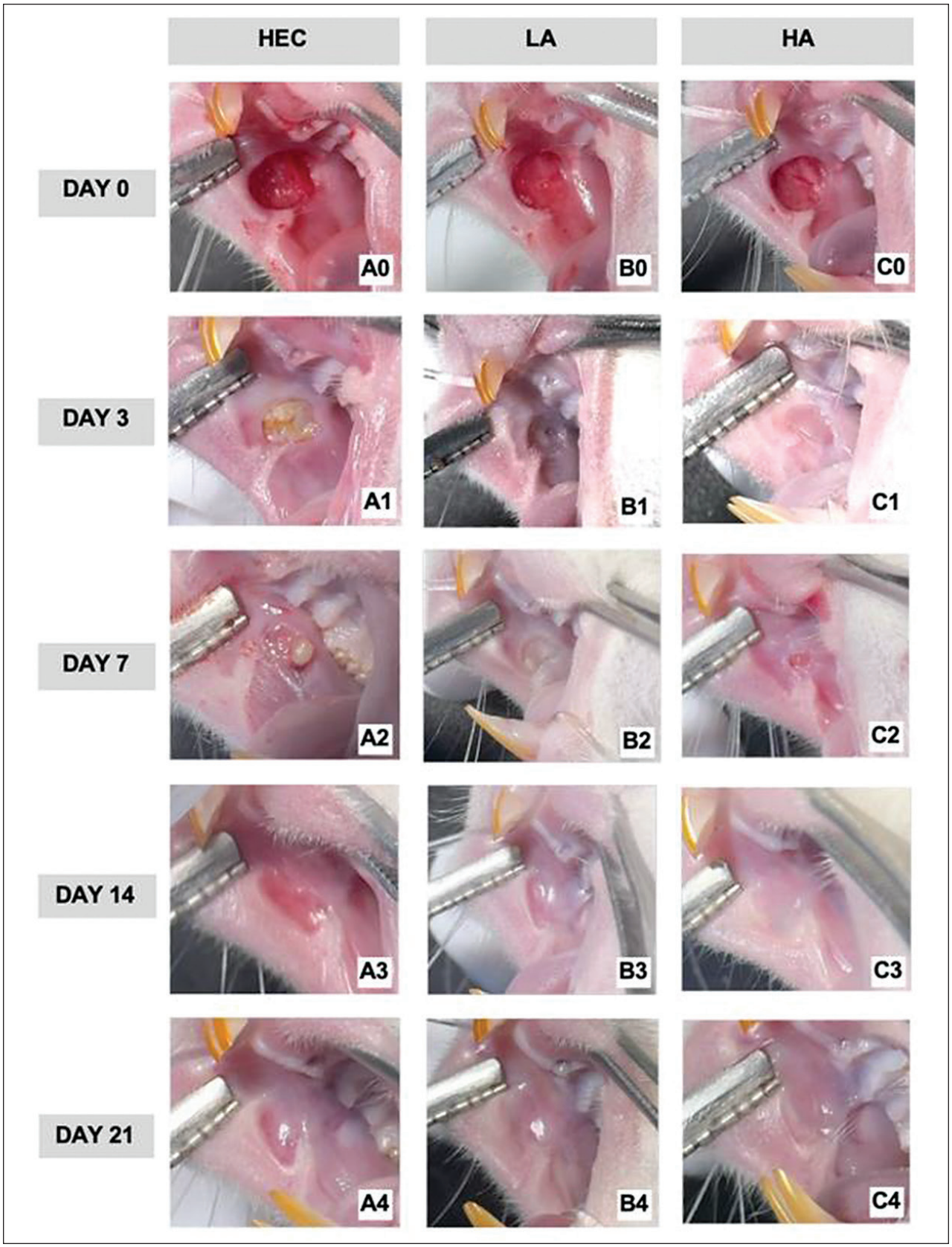

Figure 1. Macroscopic images from each group (HEC, LA, HA) at different experimental time points (Day 3, 7, 14, 21) were used for wound evaluation. HI and PAR results indicated visible changes and a reduction in wound area over time.

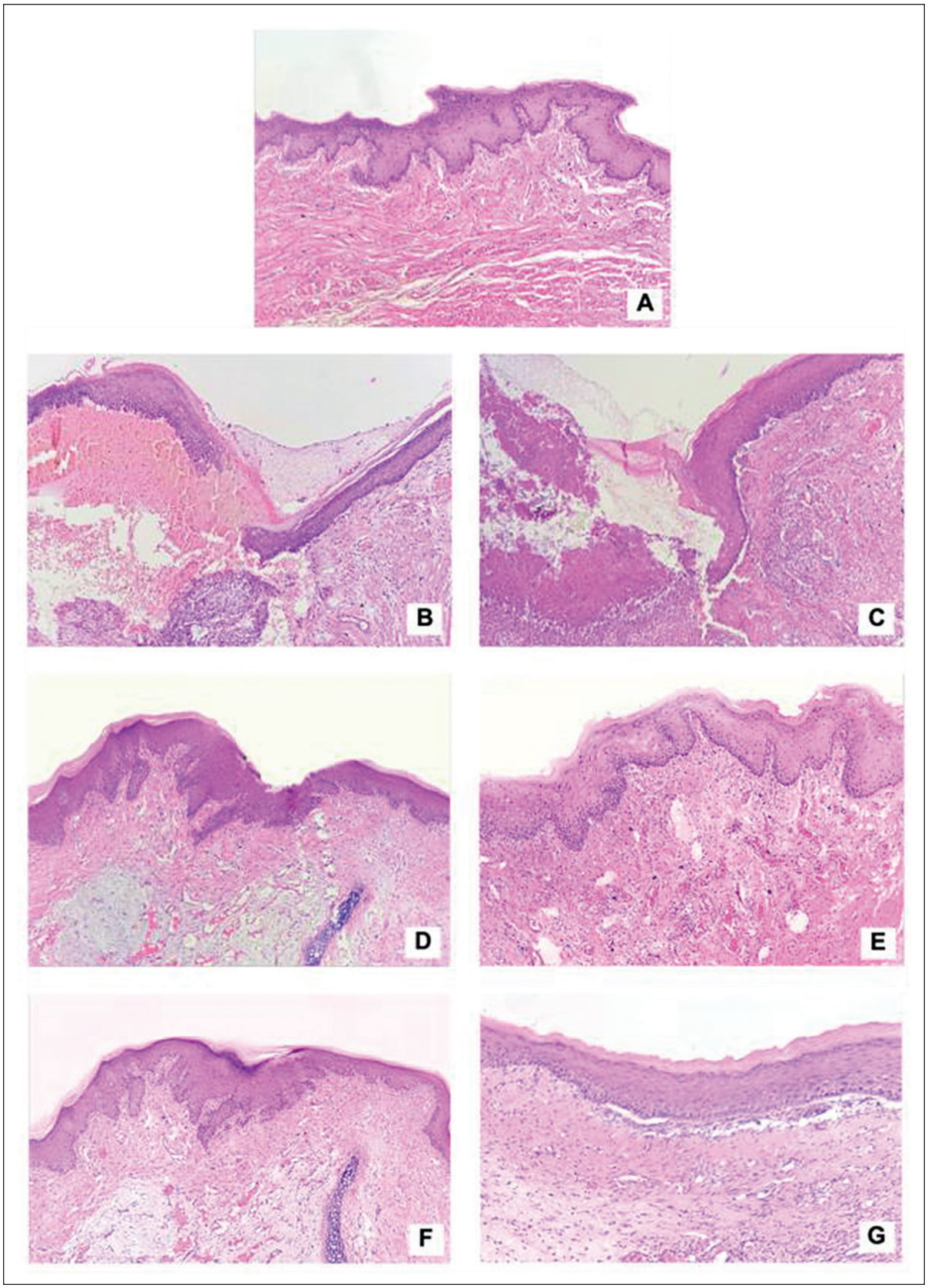

Figure 2. Histologic sections (H&E, 10x/0.25 magnification) of specimens at different experimental time points. **(A)** No Wound; **(B)** HEC Day 7, **(C)** LA Day 7, **(D)** LA Day 14, **(E)** LA Day 21, **(F)** HA Day 14, **(G)** HA Day 21.

Table 6. Summary of Histological Healing Score (HHS) Results and Kruskal-Wallis Test of Different Treatment Groups

Treatment Group	Sub-group	HHS		
		Mean ± SD	Test statistic (H)	*p*-value
HEC	A1	4.13 ± 0.35	8.47	0.0372*
	A2	6.00 ± 0.00		
	A3	6.00 ± 0.00		
	A4	6.00 ± 0.00		
LA	B1	6.00 ± 0.00	11.72	0.0084*
	B2	9.50 ± 0.93		
	B3	9.56 ± 1.25		
	B4	11.0 ± 0.00		
HA	C1	6.00 ± 0.00	8.74	0.0330*
	C2	10.63 ± 0.74		
	C3	11.00 ± 0.00		
	C4	11.00 ± 0.00		

**Statistically significant at p <0.05*

Table 7. Dunn's Test *(with Bonferroni Correction)* for Multiple Pairwise Comparisons on HHS Subgroups

Subgroups	HHS	
	Test statistic (Z)	*p*-value
A1 vs. B1	-2.353	0.056
A1 vs. C1	-2.353	0.056
B1 vs. C1	0.000	1.000
A2 vs. B2	-2.941	0.003*
A2 vs. C2	-2.991	0.003*
B2 vs. C2	-1.275	0.202
A3 vs. B3	-2.991	0.003*
A3 vs. C3	-2.941	0.003*
B3 vs. C3	-1.177	0.239
A4 vs. B4	-2.353	0.017*
A4 vs. C4	-2.353	0.017*
B4 vs. C4	0.000	1.000

**Statistically significant at p <0.05*

inflammatory infiltrates histologically (Figures 2D and 2E); however, the mean histological score of the C3 subgroup was still higher than that of the B3 subgroup, although the difference was not statistically significant. Notably, the B3 subgroup had a slightly lower mean histological score than the B2 subgroup (g = -0.05, 95% CI [-1.03, 0.93]). By contrast, the A3 subgroup showed fair wound healing, with a mean HHS of 6.00 ± 0.00, which differed significantly from that of the C3 subgroup.

On day 21, the animals assigned to the vehicle group consistently showed fair healing (HHS = 6.00 ± 0.00). In contrast, those in the experimental and positive control groups exhibited excellent wound healing and had a higher histologic score (HHS = 11.00 ± 0.00). A post hoc Dunn's test further confirmed that subgroups A4 and B4, as well as A4 and C4, were statistically different. Representative histologic sections of B4 (Figure 2F) and C4 (Figure 2G) groups also demonstrated a reorganized, intact epithelium overlying a fibrous tissue, with decreased vascularity. In Figure 2G, however, a non-intact basement membrane was observed. The separation in the basement membrane from the epithelium, however, must be interpreted with caution as the wound appears to have good wound healing, and the separation may be a histologic processing-related artifact.[23]

Since there is no significant difference between subgroups B2 and C2, B3 and C3, and B4 and C4, it can be inferred that the effects of lauric acid and hyaluronic acid on soft tissue wound healing at specific experimental time points are histologically comparable.

DISCUSSION

The findings from this study suggest that lauric acid had a positive effect on soft tissue wound healing in Sprague-Dawley rats. Results showed that subgroups treated with lauric acid had higher HI, PAR, and HHS values than subgroups without the active ingredient. However, the values observed in the lauric acid groups were not consistently higher than those of the hyaluronic acid groups at any point during the study. The findings also demonstrated no statistically significant difference between lauric acid and hyaluronic acid. Since no significant difference was observed between the experimental and positive control groups, these results indicate that the effect of lauric acid on soft tissue wound healing was clinically and histologically comparable to that of hyaluronic acid.

Soft tissue wounds in the oral cavity, like any other injury in the body, change over time as they pass through the different, yet overlapping, phases of healing.[3,25] Many treatments are also designed to optimize the conditions for natural healing, thereby causing the wound to change and progress through the phases more quickly and effectively.[26] Healing in the oral mucosa is typically faster than in the skin, as the oral cavity has a rich vascular network that helps deliver essential nutrients and oxygen to the wound site, thereby accelerating the healing process, often without the need for additional medicinal intervention.[27] However, the healing of oral wounds may be influenced by factors such as saliva, oral bacteria, and mouth movement.[3,4] Some wounds in the oral cavity also experience delayed or impaired healing and do not respond adequately to conventional treatment, posing a greater challenge for treatment and management.[5] Therefore, there is a demand for methods and materials that can accelerate the healing process for all patients, whether they are immunocompromised or not.

Lauric acid, the naturally occurring fatty acid in coconut oil and a staple in many traditional Pacific and Asian diets, has been studied for its health benefits and potential use as

a medicine; however, only a few studies, most of which are dermatological, have examined its topical effects at different concentrations.[11,28-31] In this present study, the 10% lauric acid gel concentration was used based on safety considerations and preliminary formulation testing. Safety assessments have reported that topical preparations containing 1–19.4% lauric acid are within acceptable safe-use limits, providing a basis for evaluating concentrations within this range.[32] Three concentrations (5%, 10%, and 15%) were initially formulated and evaluated for their physical properties. Among these, the 10% lauric acid gel demonstrated the most favorable characteristics, including a homogeneous and stable gel matrix, improved consistency, better spreadability, and uniform distribution of the active ingredient within the hydroxyethyl cellulose (HEC) base. In comparison, the 5% formulation exhibited high viscosity, whereas the 15% formulation produced grainy, non-uniform dispersions, suggesting poor incorporation of lauric acid. Therefore, the 10% concentration was selected for the bioassay because it provided sufficient stability, uniformity, and applicability for topical application.

Clinical and Macroscopic Wound Healing

Currently, several methods are used to assess the overall appearance of a wound at a macroscopic level, and one of the most commonly used is the Healing Index (HI) by Landry, Turnbull, and Howley. This 5-level scoring system quantifies wound healing, with higher scores indicating better healing.

The results of the study showed that the HI score of the experimental (LA) group was consistently higher than that of the vehicle control (HEC) group. Even at different experimental time points, the scores obtained by the subgroups in the LA group were higher, and on certain days, resembled those of the positive control (HA) subgroup. However, statistical analysis showed that the HI scores of subgroups at the same experimental time point but receiving different treatments revealed no significant differences. This indicated that, at a macroscopic level, soft tissue wound healing was similar across the groups at the same experimental time point, regardless of the treatment.

The clinical appearance of wounds can vary based on factors such as the type, location, depth, and severity of the injury.[33] It changes over time because it directly reflects the body's natural healing process and possibly the effects of therapeutic interventions. However, in the early stages, they often look similar because the inflammatory phase, which begins within 24 hours of the injury, can last for up to two weeks.[34] In this study, since healthy animals were used and the healing index (HI) was based only on the visual appearance of the wound, any treatment not potent enough to significantly impact the healing process would appear similar to the control group. Although the LA and HA groups were expected to exhibit better HI scores, the effect of lauric acid was probably too small to produce a statistically significant difference.

The absence of significant differences in Healing Index (HI) scores across experimental time points may reflect the inherent limitations of HI as a clinical assessment tool. HI primarily evaluates wound characteristics such as color, the presence or absence of granulation tissue, and epithelialization, making it less sensitive to subtle biological and structural changes within the healing tissue. Moreover, the semi-quantitative and ordinal nature of the scoring system may not capture minor treatment-induced improvements detectable with more sensitive methods. Another factor that may have contributed to the HI results across treatment groups was the use of two independent calibrated examiners for wound assessment. Although calibration was performed to improve scoring consistency, subtle differences in interpretation may have arisen when evaluating the different clinical wound parameters. When the soft tissue wounds exhibited only minor visible differences, both examiners may have assigned similar scores despite underlying biological variations in tissue healing. Therefore, the lack of significant differences in HI scores across subgroups of the same experimental time point does not necessarily indicate an absence of the effect of lauric acid on wound healing. Rather, the findings suggest that treatment-related improvements in wound contraction and tissue architecture were more readily detected by histologic and quantitative assessments than by gross clinical examination alone.

On the other hand, the HI scores of subgroups within the same treatment group at different experimental time points were equal to or higher than those at the previous time point and showed statistically significant differences, demonstrating that wound healing varied across experimental time points and aligns with the well-established, predictable phases of wound healing. In this study, day 3 corresponded to the inflammatory phase, during which the wound site was characterized by erythema, edema, and the presence of exudates. Accordingly, HI scores were lower at this time point, particularly in the HEC group. By day 7, clinical signs of inflammation had begun to subside, and the appearance of granulation tissue indicated a transition toward the proliferative phase. Although HI scores remained relatively low, they were higher than observed on day 3, indicating progression in the wound healing process. Finally, days 14 and 21 corresponded to the proliferative and early maturation phases of healing, during which the wound surface became fully epithelialized, erythema progressively diminished, and the newly formed tissue increasingly resembled the surrounding oral mucosa. These clinical improvements were reflected by higher HI scores, particularly in the LA and HA groups, indicating enhanced wound healing and tissue maturation over time.

Wound contraction has been widely recognized as a key component of both cutaneous and oral wound healing, as it facilitates a reduction in wound size.[35] In addition to contributing to physical wound closure, it serves as an important clinical parameter for evaluating the progression

of healing and for assessing the therapeutic effects of interventions.[36] Previous reports have suggested that quantifying wound contraction after four weeks of treatment provides a reliable estimate of healing potential, with a 50% reduction in wound area at this time point often considered a meaningful indicator of favorable healing outcomes.[37] In this study, Percentage Area Reduction or PAR was used as a clinical parameter of wound healing; that is, the greater the PAR, the greater wound healing effect is observed.

Soft tissue wounds, such as oral aphthous ulcers, typically heal naturally within a few days; however, complete resolution of larger lesions may require up to six weeks or longer.[38] In this study, the HEC group did not achieve complete wound closure by the end of the third week. In contrast, the LA group demonstrated a progressive reduction in wound area, with approximately 55% PAR observed by day 3, 98% by day 14, and complete closure by day 21. Notably, the hyaluronic acid-treated group exhibited an even more pronounced effect, achieving 100% PAR as early as the second week, indicating more rapid wound contraction compared with the other treatment groups.

Several studies have demonstrated that hyaluronic acid enhances oral wound healing through multiple mechanisms, including modulation of inflammation, antimicrobial activity, maintenance of a moist wound environment, and promotion of re-epithelialization.[39-42] These effects collectively facilitate faster tissue repair and more organized epithelial coverage of the wound surface. Similarly, lauric acid has been reported to possess anti-inflammatory and antimicrobial properties and to accelerate epithelial wound closure by enhancing the proliferation and migration of keratinocytes and other cells at wound margins, thereby promoting the more rapid re-establishment of the epithelial barrier and accelerating the wound healing process.[43] In this study, the absence of a statistically significant difference in PAR between the lauric acid and hyaluronic acid groups suggests that both treatments exerted comparable effects in promoting soft tissue wound healing and contraction. This finding also implies that lauric acid may exhibit a similar wound healing effect to that of hyaluronic acid, at least in terms of macroscopic wound reduction.

Histologic Wound Healing

Histologic examination is a valuable method for assessing wound healing because it enables direct visualization of cellular and tissue-level changes that are not readily detectable by gross clinical observation.[2] It provides detailed information on inflammatory cell activity, fibroblast proliferation, collagen deposition, angiogenesis, and epithelial organization, thereby enabling a more sensitive evaluation of the wound healing process.[44] In this study, the histologic state of the wound was assessed using the Histologic Healing Score (HHS), a scoring system that evaluates key parameters, specifically the amount of inflammatory infiltrates and granulation tissue, and the pattern and orientation of collagen fibers.[45,46]

Successful wound healing is reflected by decreased inflammatory cell infiltration and granulation tissue, and more aligned, uniform collagen fibers, indicating the transition from active inflammation to tissue repair and maturation.[47] Inflammatory cells like neutrophils and macrophages are typically involved in the inflammatory phase of wound healing.[5] These cells gather at the wound site, and once the wound is cleared of pathogens and damaged tissue, the cells release chemical mediators, signaling the next phase of wound healing.[48] Granulation tissue, characterized by the presence of new blood vessels, fibroblasts, and collagen, forms and increases during the proliferative phase. In general, a decrease in the amount of granulation tissue is considered indicative of improved progression toward the remodeling phase of wound healing, as mature healing tissue is characterized by reduced cellular proliferation and increased organization of the extracellular matrix.[2,49] Evaluation of collagen fiber pattern and orientation also served as an indicator of the degree of tissue maturation and remodeling during the later stages of wound healing, as more organized and well-aligned collagen fibers reflect improved structural integrity of the newly formed tissue. [2,50]

The study demonstrated an increase in Histologic Healing Score (HHS) over time, indicating progressive wound healing across all groups. From day 0 (Figure 2A) until day 21, wounds treated with LA and HA consistently exhibited higher scores than the HEC group, reflecting a relative reduction in inflammatory cell infiltration and granulation tissue formation. Statistical analysis further revealed that the LA and HA groups were comparable to each other across the evaluated histologic parameters, while both differed significantly from the HEC group. In contrast, evaluation of collagen fiber pattern and orientation showed no statistically significant differences among the treatment groups, suggesting a similar degree of collagen organization and maturation across all interventions.

Studies on lauric acid have reported that its antimicrobial property positively affects wound healing by reducing the bacterial load and helping maintain a relatively clean environment necessary for the healing process.[51] In addition, its aseptic and regenerative effects have been shown to further support the healing process by modulating inflammatory responses and promoting tissue regeneration.[52] Histologically, these effects are expected to manifest as a decrease in inflammatory cell infiltration.

It was also consistent with the findings of a recent review, which reported that lauric acid demonstrated excellent healing and promoted cell migration and proliferation of human gingival fibroblasts.[29] From a histologic perspective, these may be reflected by increased fibroblast activity within the wound bed, contributing to more rapid granulation tissue formation in the early proliferative stage, as well as re-epithelialization.

Similar to lauric acid, hyaluronic acid is an important bioactive compound used in many therapeutic applications,

particularly in wound management.[53,54] Notably, some of its biological effects are comparable with those of lauric acid, which may help explain why the HHS observed between the two treatment groups is statistically similar, particularly from days 7 and 21. Although existing studies suggest that lauric acid can also help reduce inflammation and recruit inflammatory cells to the wound site, which are likewise attributed to hyaluronic acid, its direct influence on wound healing at a histological level remains less extensively characterized and still requires further investigation.[29,55]

The present study examined the effect of lauric acid on soft tissue wound healing in Sprague-Dawley rats at both clinical and histological levels; however, immunological and biochemical parameters associated with soft tissue wound healing were not assessed. In addition, the experiment was limited to 21 days; therefore, the long-term effects and stabi-lity of lauric acid gel remain unexamined. The study also investigated a single formulation, specifically a gel containing 10% lauric acid; thus, other concentrations were not studied, and the optimal therapeutic dose for wound healing remains to be determined. Furthermore, additional quality control tests, such as acute toxicity, mucoadhesion, pharmacological profiling, and drug release kinetics, are recommended to fully support the findings of this study and to validate and strengthen the applicability of the formulation for clinical use.

Given that the findings from this study indicate a positive effect of lauric acid on soft tissue wound healing and considering that it comprises the majority of the fatty acids in coconut oil, the results of this study may further contribute to the existing literature supporting the therapeutic effects of coconut oil and coconut-derived products. Moreover, future research may utilize the findings of this study to develop a lauric acid-based formulation as an alternative treatment for soft tissue wounds and other oral mucosal injuries in the human oral cavity.

CONCLUSION

The results indicated that the application of lauric acid has an effect and promotes healing of soft tissue wounds in the buccal mucosa of Sprague-Dawley rats. Furthermore, the healing of soft tissue wounds treated with lauric acid was comparable to that of hyaluronic acid, both clinically and histologically.

Acknowledgments

The authors gratefully acknowledge Dr. Roan S. Pechayco, Dr. Aaron E. Tuazon, and Dr. Maria Jacinta Rosario H. Romero from the Department of Clinical Dental Health Sciences, College of Dentistry, University of the Philippines Manila, Mr. Billy Atendido from the Multidisciplinary Laboratory of the UP College of Medicine, and Ms. Ednorimae Q. Guico, Ms. Divina G. Dacudag, Ms. Monique B. Mandap, and Ms. Lota E. Yonson, for their support and expertise that made this research possible. Special appreciation is also given to UPCD Dean, Dr. Michelle C. Sunico-Segarra, for her invaluable support and guidance.

Statement of Authorship

All authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

All authors declared no conflicts of interest.

Funding Source

This study was fully funded by the authors. No private funding or institutional financial support was received for the completion of this study.

REFERENCES

1. Anura A. Traumatic Oral Mucosal Lesions: A Mini Review And Clinical Update. Oral Health Dent Manag. 2014 Jun;13(2):254-9. PMID: 24984629.
2. Guo S, Dipietro L. Factors Affecting Wound Healing. J Dent Res. 2010 Mar;89(3):219-29. doi: 10.1177/0022034509359125. PMID: 20139336. PMCID: PMC2903966.
3. Toma A, Fuller J, Willett N, Goudy S. Oral wound healing models and emerging regenerative therapies. Transl Res. 2021 Oct;236: 17-34. doi: 10.1016/j.trsl.2021.06.003. PMID: 34161876. PMCID: PMC8380729.
4. Leskow N, Karp Z, Banaszewski M, Popielska K, Grzeskowiak M, Mikołajski J, et al. Characteristics and cellular mechanism of the wound healing process in the oral mucosa. Med J Cell Biol. 2023 Aug; 11(1):1-12. doi:10.2478/acb-2023-0001.
5. Brizeno L, Assreuy A, Alves A, Sousa F, Silva P, Sousa S, et al. Delayed healing of oral mucosa in a diabetic rat model: Implication of TNF-α, IL-1β, and FGF-2. Life Sci. 2016 May; 155:36-47. doi: 10.1016/j.lfs.2016.04.033
6. Lorusso F, Gianluca N, Scarano A. Clinical efficacy of a topical gel for the treatment of minor oral ulcers: A triple-blind randomized controlled trial. Appl Sci. 2025 Jun;15(13):7347. doi: 10.3390/app15137347
7. Khalil H, Cullen M, Chambers H, McGrail M. Medications affecting healing: an evidence-based analysis. Int Wound J. 2017 Dec;14(6):1340-1345. doi: 10.1111/iwj.12809. PMID: 28944576; PMCID: PMC7949850.
8. Moses R, Prescott T, Mas-Claret E, Steadman R, Moseley R, Sloan AJ. Evidence for natural products as alternative wound-healing therapies. Biomolecules. 2023 Feb;13(3):444. doi: 10.3390/biom13030444. PMID: 36979379; PMCID: PMC10046143.
9. Dayrit F. The properties of lauric acid and their significance in coconut oil. J Am Oil Chem Soc. 2015 Jan;92(1):1-15. doi: 10.1007/s11746-014-2562-7
10. Nitbani F, Tjitda P, Nitti F, Jumina J, Detha A. Antimicrobial properties of lauric acid and monolaurin in virgin coconut oil: a review. Chembioeng Rev. 2022 Jun;9(5):442-61. doi: 10.1002/cben.202100050
11. Ameena M, Arumugham M, Ramalingam K, Shanmugam R. Biomedical applications of lauric acid: a narrative review. Cureus. 2024 Jun;16(6):e62770. doi: 10.7759/cureus.62770. PMID: 39036266. PMCID: PMC11260118.
12. Hickman D, Swan M. Use of a body condition score technique to assess health status in a rat model of polycystic kidney disease. J Am Assoc Lab Anim Sci. 2010 Mar;49(2):155-9. PMID: 20353688; PMCID: PMC2846001.

13. Navarro K, Huss M, Smith J, Sharp P, Marx J, Pacharinsak C. Mouse Anesthesia: The Art and Science. ILAR J. 2021 Dec 31;62(1-2): 238-273. doi: 10.1093/ilar/ilab016. PMID: 34180990; PMCID: PMC9236661.
14. Olsson IA, Dahlborn K. Improving housing conditions for laboratory mice: a review of "environmental enrichment". Lab Anim. 2002 Jul; 36(3):243-70. doi: 10.1258/002367702320162379. PMID: 12144738.
15. Bayne K, Morris T, France M. The UFAW handbook on the care and management of laboratory and other research animals. 8th ed. Chichester (UK): Wiley-Blackwell; 2010. doi:10.1002/9781444318777.ch8.
16. Ferrari L, Turrini G, Rostello C, Guidi A, Casartelli A, Piaia A, Sartori M. Evaluation of two combinations of Domitor, Zoletil 100, and Euthatal to obtain long-term nonrecovery anesthesia in Sprague-Dawley rats. Comp Med. 2005 Jun;55(3):256-64. PMID: 16089174.
17. Cavalcante G, Sousa de Paula R, Souza L, Sousa F, Mota M, Alves A. Experimental model of traumatic ulcer in the cheek mucosa of rats. Acta Cir Bras. 2011 Jun;26(3):227-34. doi: 10.1590/s0102-86502011000300012. PMID: 21537526.
18. Mortazavi H, Mashhadiabbas F, Mortazavi SAR, Rezaeifar K, Farhangi M. Formulation of a Jasmine Grandiflorum containing mucoadhesive and evaluation of its healing effect on oral biopsy ulcers. Clin Oral Investig. 2020 Apr;24(4):1591-1597. doi: 10.1007/s00784-019-03171-w. PMID: 31916035.
19. Silva P, De Codes É, Freitas M, Martins J, Alves A, Sousa F. Experimental model of oral ulcer in mice: Comparing wound healing in three immunologically distinct animal lines. J Oral Maxillofac Pathol. 2018 Sep-Dec;22(3):444. doi: 10.4103/jomfp.JOMFP_144_17. PMID: 30651700; PMCID: PMC6306613.
20. Oakley A. Topical formulations [Internet]. Hamilton (NZ): DermNet NZ; 2016 Feb [updated 2016 Feb; cited 2024 Jun 21]. Available from: https://dermnetnz.org/topics/topical-formulations
21. Kumar A, Clover A. Intraperitoneal co-administration of low dose urethane with xylazine and ketamine for extended duration of surgical anesthesia in rats. Lab Anim Res. 2015 Dec;31(4):174-9. doi: 10.5625/lar.2015.31.4.174. PMID: 26755920. PMCID: PMC4707145.
22. Rodriguez A, Alhachache S, Velasquez D, Chan H. A systematic review of oral wound healing indices. PLoS One. 2024 Feb 8;19(2): e0290050. doi: 10.1371/journal.pone.0290050. PMID: 38330054. PMCID: PMC10852230.
23. Foltynski P, Ladyzynski P, Ciechanowska A, Migalska-Musial K, Judzewicz G, Sabalinska S. Wound Area Measurement with Digital Planimetry: Improved Accuracy and Precision with Calibration Based on 2 Rulers. PLoS One. 2015 Aug 7;10(8):e0134622. doi: 10.1371/journal.pone.0134622. PMID: 26252747. PMCID: PMC4529141.
24. Sultana J, Molla M, Kamal M, Shahidullah M, Begum F, Bashar M. Histological differences in wound healing in maxillofacial region in patients with or without risk factors. Bangladesh J Pathol. 2009 Jul;24(1):3-8. doi: 10.3329/bjpath.v24i1.2874
25. Waasdorp M, Krom BP, Bikker FJ, van Zuijlen PPM, Niessen FB, Gibbs S. The Bigger Picture: Why Oral Mucosa Heals Better Than Skin. Biomolecules. 2021 Aug 6;11(8):1165. doi: 10.3390/biom11081165. PMID: 34439831; PMCID: PMC8394648.
26. Capodiferro S, Tempesta A, Bucci S, Maiorano E, Favia G, Limongelli L. Aminogam Gel Allows Faster Wound Healing after Oral Surgery by Formation of Mature Connective Tissue with Low Vascular Density and Reducing Inflammatory Infiltration. A Retrospective Study on 580 Cases with Histological and Confocal Laser Investigation. Appl Sci. 2020 Feb;10(3):1105. doi: 10.3390/app10031105
27. Pilloni A, Marini L, Gagliano N, Canciani E, Dellavia C, Cornaghi L, et al. Clinical, histological, immunohistochemical, and biomolecular analysis of hyaluronic acid in early wound healing of human gingival tissues: A randomized, split-mouth trial. J Periodontol. 2023 Jul;94(7):868-881. doi: 10.1002/JPER.22-0338. PMID: 36648006.
28. Patil U, Benjakul S. Coconut Milk and Coconut Oil: Their Manufacture Associated with Protein Functionality. J Food Sci. 2018 Aug;83(8):2019-2027. doi: 10.1111/1750-3841.14223. PMID: 30004125.
29. Ameena M, Arumugham M, Ramalingam K, Rajeshkumar S, Perumal E. Cytocompatibility and Wound Healing Activity of Chitosan Thiocolchicoside Lauric Acid Nanogel in Human Gingival Fibroblast Cells. Cureus. 2023 Aug;15(8):e43727. doi: 10.7759/cureus.43727. PMID: 37727182; PMCID: PMC10505684.
30. International Bio-Research US. Acute toxicity and irritation studies on a series of fatty acids: high purity stearic acid, triple pressed stearic acid, lauric acid, oleic acid, myristic acid and palmitic acid [report]. 1974.
31. Cosmetic, Toiletry and Fragrance Association (CTFA). Primary skin irritation data summary sheet on lauric acid [report]. 1978.
32. Cosmetic Ingredient Review, Safety assessment of fatty acid and fatty acid salts as used in cosmetics [Internet]. 2019 [cited 2026 April]. Available from: https://cir-reports.cir-safety.org/view-attachment/?id=3a3ac6dd-8c74-ec11-8943-0022482f06a6.
33. Hammerle C, Giannobile W; Working Group 1 of the European Workshop on Periodontology. Biology of soft tissue wound healing and regeneration--consensus report of Group 1 of the 10th European Workshop on Periodontology. J Clin Periodontol. 2014 Apr;41 Suppl 15:S1-5. doi: 10.1111/jcpe.12221. PMID: 24640995.
34. Fitridge R, Thompson M. Mechanisms of Vascular Disease: A Reference Book for Vascular Specialists [Internet]. Adelaide (AU): University of Adelaide Press; 2011 [cited 2025 Sep]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK534260/
35. Horan M, Quan N, Subramanian S, Strauch A, Gajendrareddy P, Marucha P. Impaired wound contraction and delayed myofibroblast differentiation in restraint-stressed mice. Brain Behav Immun. 2005 May;19(3):207-16. doi: 10.1016/j.bbi.2004.09.004. PMID: 15797309.
36. Al-Akayleh F, Jaber N, Al-Remawi M, Al Odwan G, Qinna N. Chitosan-biotin topical film: preparation and evaluation of burn wound healing activity. Pharm Dev Technol. 2022 Apr;27(4):479-489. doi: 10.1080/10837450.2022.2079132. PMID: 35575443.
37. Coerper S, Beckert S, Kuper M, Jekov M, Konigsrainer A. Fifty percent area reduction after 4 weeks of treatment is a reliable indicator for healing--analysis of a single-center cohort of 704 diabetic patients. J Diabetes Complications. 2009 Jan-Feb;23(1):49-53. doi: 10.1016/j.jdiacomp.2008.02.001. PMID: 18394932.
38. Mortazavi H, Namazi F, Badiei M, Bakhshi M. Evaluation of therapeutic effects of Adcortyl and Myrtus communis (Myrtle) in patients with recurrent aphthous stomatitis: a clinical trial study. Healthmed. 2012 Jan;6(5):1693-1698.
39. Lee J, Lee K, Nam O, Chae Y, Lee M, Kweon D, et al. Orodispersible hyaluronic acid film delivery for oral wound healing in rats. J Dent Sci. 2022 Oct;17(4):1595-1603. doi: 10.1016/j.jds.2022.04.004. PMID: 36299335; PMCID: PMC9588893.
40. Cankaya Z, Gurbuz S, Bakirarar B, Unsal B, Kurtis B. Evaluation of the effect of the application of hyaluronic acid following laser-assisted frenectomy: an examiner-blind, randomized, controlled clinical study. Quintessence Int. 2020;51(3):188-201. doi: 10.3290/j.qi.a43667. PMID: 31781694.
41. Yildirim S, Ozener H, Dogan B, Kuru B. Effect of topically applied hyaluronic acid on pain and palatal epithelial wound healing: An examiner-masked, randomized, controlled clinical trial. J Periodontol. 2018 Jan;89(1):36-45. doi: 10.1902/jop.2017.170105. PMID: 28914592.
42. Antoszewska M, Sokolewicz E, Baranska-Rybak W. Wide use of hyaluronic acid in the process of wound healing—A rapid review. Sci Pharm. 2024 Apr;92(2):23. doi:10.3390/scipharm92020023
43. Mustafa A, Arumugham Indiran M, Shanmugham R, Ramalingam K. Anti-inflammatory activity of lauric acid, thiocolchicoside and thiocolchicoside-lauric acid formulation. Bioinformation. 2023 Nov;19(11):1075-1080. doi: 10.6026/973206300191075. PMID: 38046516; PMCID: PMC10692977.
44. Eming SA, Krieg T, Davidson JM. Inflammation in wound repair: molecular and cellular mechanisms. J Invest Dermatol. 2007 Mar; 127(3):514-25. doi: 10.1038/sj.jid.5700701. PMID: 17299434.

45. Gupta A, Kumar P. Assessment of the histological state of the healing wound. Plast Aesthet Res. Sep 2015;2:239-42. doi: 10.4103/2347-9264.158862
46. Santoso A, Amalia E, Sari K, Takarini V, Sufiawati I. Histopathological Evaluation of Wound Healing and Anti-Inflammatory Effects of Granola Potato Peel Ethanol Extract in Rat Oral Mucosa. J Exp Pharmacol. 2024 Oct 24;16:377-395. doi: 10.2147/JEP.S487373. PMID: 39469135. PMCID: PMC11514816.
47. Stupin V, Manturova N, Silina E, Litvitskiy P, Vasin V, Artyushkova E, et al. The Effect of Inflammation on the Healing Process of Acute Skin Wounds Under the Treatment of Wounds with Injections in Rats. J Exp Pharmacol. 2020 Oct;12:409-422. doi: 10.2147/JEP.S275791. PMID: 33154679; PMCID: PMC7608486.
48. Krzyszczyk P, Schloss R, Palmer A, Berthiaume F. The Role of Macrophages in Acute and Chronic Wound Healing and Interventions to Promote Pro-wound Healing Phenotypes. Front Physiol. 2018 May; 9:419. doi: 10.3389/fphys.2018.00419. PMID: 29765329; PMCID: PMC5938667.
49. Gurtner GC, Werner S, Barrandon Y, Longaker MT. Wound repair and regeneration. Nature. 2008 May 15;453(7193):314-21. doi: 10.1038/nature07039. PMID: 18480812.
50. Diegelmann RF, Evans MC. Wound healing: an overview of acute, fibrotic and delayed healing. Front Biosci. 2004 Jan 1;9:283-9. doi: 10.2741/1184. PMID: 14766366.
51. Bobinski R, Wyszomirski M, Machnickam A, Pielesz A, Kawecki M, Waksmanska W, et al. The Effect of Lauric Acid on Pathogens Colonizing the Burn Wound: A Pilot Study. Altern Ther Health Med. 2020 Mar;26(2):23-27. PMID: 31634869.
52. Lieberman S, Enig M, Preuss H. A Review of Monolaurin and Lauric Acid: Natural Virucidal and Bactericidal Agents. Alternative and Complementary Therapies. 2006 Dec;12:310-4. doi: 10.1089/act.2006.12.3
53. Fallacara A, Baldini E, Manfredini S, Vertuani S. Hyaluronic Acid in the Third Millennium. Polymers (Basel). 2018 Jun 25;10(7): 701. doi: 10.3390/polym10070701. PMID: 30960626; PMCID: PMC6403654.
54. Frenkel JS. The role of hyaluronan in wound healing. Int Wound J. 2014 Apr;11(2):159-63. doi: 10.1111/j.1742-481X.2012.01057.x. PMID: 22891615; PMCID: PMC7950635.
55. Thangavel P, Saravanakumar I, Sundaram M, Balavigneswaran C, Balamurugan R, Muthuvijayan V. Lauric acid-loaded biomimetic, biocompatible, and antioxidant jelly fig (Ficus awkeotsang Makino) pectin hydrogel accelerates wound healing in diabetic rats. Int J Biol Macromol. 2025 Mar;294:139484. doi: 10.1016/j.ijbiomac.2025.139484. PMID: 39756728.