Effectiveness of a Mucoadhesive Patch Containing Cinnamon Leaf (Cinnamomum burmannii) Extract as an Alternative Therapy for Traumatic Ulcers in Wistar Rats

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Abstrak

Background: *Traumatic ulcers are common oral mucosal lesions caused by local trauma and generally heal spontaneously after elimination of the causative factor. Mucoadhesive patches may provide prolonged contact with the ulcer surface and facilitate localized delivery of active compounds. Cinnamon leaf (Cinnamomum burmannii) contains bioactive compounds with anti-inflammatory and wound-healing potential. This study evaluated the effectiveness of a mucoadhesive patch containing Cinnamomum burmannii leaf extract in reducing the diameter of traumatic ulcers in Wistar rats.*

Method: *A true experimental study using a Posttest-Only Control Group Design was cnducted on eighteen male Wistar rats, which were randomly allocated to three groups: Positive control group treated with Aloclair® gel (K+), Mucoadhesive patch containing 35% Cinnamomum burmannii leaf extract formulated with HPMC and Carbopol® 940P (P), and Negative control group treated with a placebo mucoadhesive patch (K-). Ulcer diameters were measured on days 1, 3, 5, 7, and 10. Data were analyzed using one-way ANOVA followed by Bonferroni post hoc testing.*

Result: *The mucoadhesive patch containing Cinnamomum burmannii leaf extract showed no significant difference in ulcer diameter compared with the placebo group on days 1, 3, and 5 ($p > 0.05$). A significant difference was observed on day 7, with the treatment group showing a smaller ulcer diameter than the placebo group ($p < 0.05$). On day 7, no significant difference was observed between the treatment and Aloclair® groups ($p > 0.05$). Both the treatment and positive control groups achieved complete healing by day 10.*

Conclusion: *The mucoadhesive patch containing Cinnamomum burmannii leaf extract demonstrated a significant reduction in traumatic ulcer diameter compared with the placebo patch on day 7 and showed a healing outcome comparable to Aloclair® gel at that observation point. These findings indicate that the cinnamon leaf extract mucoadhesive patch has potential*

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INTRODUCTION

Traumatic ulcer is an ulcerative lesion of the oral mucosa caused by local trauma. Common etiological factors include accidental biting of the oral mucosa, improper toothbrushing techniques, ill-fitting orthodontic appliances, consumption of excessively hot foods or beverages, and the use of mouthwashes containing high concentrations of alcohol. Clinically, traumatic ulcers are characterized by inflammatory signs, including redness caused by capillary dilation (*rubor*), warmth (*calor*), pain (*dolor*), swelling (*tumor*), and impaired function (*functio laesa*), all of which contribute to patient discomfort[1]. Globally, oral ulcers affect approximately 25% of the population, with trauma representing one of the most common causes. In Indonesia, the prevalence of oral ulcerative lesions is also relatively high. A study by Langkir et al. reported that 96.6% of 29 respondents in Minahasa Regency presented with traumatic oral lesions[2]. Traumatic ulcers are most frequently found on the buccal mucosa, lateral border of the tongue, and labial mucosa. Morphologically, these lesions may present as either deep ulcers or superficial erosions. The center of the lesion typically appears yellowish to grayish due to the presence of fibrinous exudate surrounded by an erythematous halo, with lesion diameters generally ranging from 1 to 8 mm depending on the severity and nature of the traumatic insult[3].

Traumatic ulcers generally heal spontaneously within 10–14 days after the causative factor has been eliminated, although the healing period depends on the location, duration, and size of the lesion[4]. Wound healing is a dynamic process consisting of three overlapping phases: inflammation, proliferation, and remodeling. During the inflammatory phase, macrophages release growth factors, including TGF-β, TGF-α, FGF, and VEGF, which initiate tissue repair. The proliferative phase is characterized by epithelial cell migration, fibroblast proliferation, angiogenesis, and granulation tissue formation, leading to wound closure. Finally, the remodeling phase involves extracellular matrix reorganization and fibroblast differentiation into myofibroblasts, resulting in restoration of tissue integrity[5].

Adjunctive therapyis often administered to accelerate wound healing and relieve patient discomfort. Topical anti-inflammatory agents such as Aloclair gel are widely used for the management of oral inflammatory lesions because they effectively reduce discomfort and are available without a prescription[6]. Other conventional therapies, including topical corticosteroids and antiseptic mouthwashes, have also demonstrated clinical effectiveness; however, their use may be associated with adverse effects such as mucosal irritation, disruption of the normal oral microbiota, and the potential development of antimicrobial resistance[7,8]. Therefore, the development of safer and more effective alternative therapies remains necessary.

Cinnamon leaves *(Cinnamomum burmannii)* contain various bioactive secondary metabolites, including alkaloids, flavonoids, saponins, and tannins, which possess antibacterial, antifungal, antioxidant, and anti-inflammatory activities. Flavonoids exert anti-inflammatory effects by inhibiting cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, thereby suppressing the production of inflammatory mediators and reducing inflammation[9]. In addition, flavonoids promote fibroblast proliferation and inhibit bacterial growth, thereby facilitating tissue regeneration and accelerating wound healing[10].

Mucoadhesive patches offer several advantages over conventional dosage forms. They are non-invasive, associated with minimal adverse effects, and capable of maintaining drug

bioavailability by prolonging drug residence time at the site of application. Furthermore, these patches exhibit strong adhesion to the oral mucosa, bypass first-pass metabolism, and allow immediate discontinuation of drug administration if adverse reactions occur, thereby reducing the risk of systemic toxicity[11].

Considering the pharmacological properties of *Cinnamomum burmannii* leaf extract and the therapeutic advantages of the mucoadhesive delivery system, this study was conducted to evaluate the effectiveness of a mucoadhesive patch containing *Cinnamomum burmannii* leaf extract as an alternative therapy for traumatic ulcers.

RESEARCH METHOD

This study employed a true experimental design using a Posttest-Only Control Group Design. The research has an ethical eligibility number of 1.271/VI/HREC/2025 from the Health Research Ethics Commission (KEPK), RSUD Dr. Moewardi. The study began with plant determination, which was carried out at the Traditional Health Care Unit (UPF Pelayanan Kesehatan Tradisional), Dr. Sardjito General Hospital, Tawangmangu (No.TL.02.04/D.XI.6/22199.717/2025). Plant authentication was performed through organoleptic examination.

The instruments used in this study included an analytical balance, oven, mortar and pestle, beakers, glass stirring rods, glass containers, vacuum Buchner filtration apparatus, filter paper, extraction flask, rotary evaporator, Erlenmeyer flasks, graduated cylinders, porcelain evaporating dishes, water bath, glass bottles, hot plate, Petri dishes, pH meter, biopsy punch, and a digital sliding caliper. The materials consisted of 500 g of dried *Cinnamomum burmannii* leaves, 96% ethanol, distilled water, hydroxypropyl methylcellulose (HPMC), Carbopol® 940P, Tween 80, propylene glycol, lidocaine–prilocaine cream (EMLA® 5%), xylazine, Castran®, BR-1 laboratory feed, 10% ammonia solution, hydrochloric acid (HCl), 1% ferric chloride ($FeCl_3$), and sulfuric acid (H_2SO_4).

The extraction process was carried out using the maceration method, in which the dried leaf powder was immersed in 96% ethanol at a 1:10 (w/v) ratio for three days at room temperature under light-protected conditions. The filtrate was collected by vacuum Buchner filtration and concentrated using a rotary evaporator at 70°C to obtain a liquid extract. The extract was subsequently evaporated using a water bath at the same temperature until a thick extract was obtained and then stored in an airtight container until further use.

Phytochemical screening was performed to identify the presence of bioactive compounds in the cinnamon leaf extract. Alkaloids were identified by dissolving the extract in 2 N hydrochloric acid followed by the addition of Mayer's and Dragendorff's reagents. The formation of a white to yellow precipitate indicated a positive result. Flavonoids were detected using the magnesium–hydrochloric acid reduction test after heating the extract in ethanol, with the appearance of red, yellow, or orange coloration indicating a positive reaction. Saponins were identified using the foam test, in which the formation of stable foam after vigorous shaking with hot water indicated a positive result. Tannins were detected by adding 1% ferric chloride ($FeCl_3$) solution to the heated filtrate, where the appearance of a dark bluish-black color confirmed their presence.

The mucoadhesive patch was prepared at the Pharmaceutics Laboratory of Universitas Setia Budi using the solvent casting method. Hydroxypropyl methylcellulose (HPMC) and Carbopol® 940P were separately dissolved in hot distilled water until homogeneous polymer solutions

were obtained. The two polymer solutions were then combined, followed by the incorporation of 35% *Cinnamomum burmannii* leaf extract while continuously stirring until a homogeneous mixture was achieved. Tween 80 and propylene glycol were subsequently added, and the mixture was stirred until completely homogeneous. The resulting solution was poured into Petri dishes and dried in an oven at 40°C for 24 hours, followed by conditioning at room temperature for an additional 24 hours. The dried films were cut into 3 × 3 mm patches and evaluated for their physicochemical properties, including weight uniformity, thickness uniformity, folding endurance, surface pH, and mucoadhesive strength.

The effectiveness of the mucoadhesive patch in reducing the diameter of traumatic ulcers was evaluated at the Pharmacology Laboratory, Faculty of Medicine, Universitas Muhammadiyah Surakarta. Before ulcer induction, the animals were anesthetized by intramuscular injection of a combination of xylazine (0.2 mg/kg body weight) and Castran® (0.02 mg/kg body weight) into the left thigh muscle. A standardized traumatic ulcer was then created on the labial mucosa using a 2-mm biopsy punch with a depth of 1 mm. Following ulcer induction, each animal received the assigned treatment according to its respective group. Ulcer healing was evaluated by measuring the ulcer diameter using a digital sliding caliper on days 1, 3, 5, 7, and 10, with all measurements performed at 4:00 p.m.

Statistical analyses were performed using IBM SPSS Statistics software. Data normality was assessed using the Shapiro–Wilk test because the sample size was fewer than 50 observations, while homogeneity of variance among groups was evaluated using Levene's test. Data were considered normally distributed and homogeneous when $p > 0.05$. Differences among groups were analyzed using one-way analysis of variance (ANOVA) with a 95% confidence level. When statistically significant differences were detected, Bonferroni's post hoc test was performed to determine pairwise differences among the treatment groups.

RESULT

The plant authentication results confirmed that the cinnamon leaves used in this study belonged to the species *Cinnamomum burmannii*. The results of the phytochemical screening of *Cinnamomum burmannii* leaf extract are presented in Table 1.

Table 1. Phytochemical Screening Results of *Cinnamomum burmannii* Leaf Extract

Active Compound	Phytochemical Test	Observation
Alkaloid	+	Light brown
Flavonoid	+	Orange
Tanin	+	Dark bluish-black
Saponin	+	Yellow with stable foam

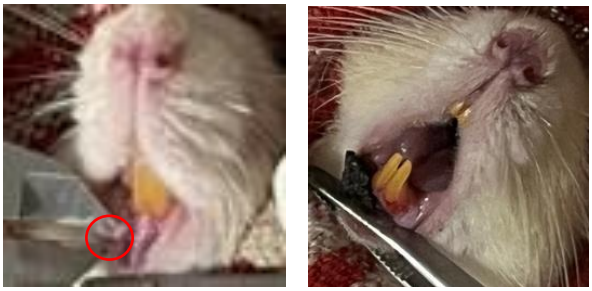
Note: (+) indicates the presence of the tested phytochemical compound.

The phytochemical screening demonstrated that *Cinnamomum burmannii* leaf extract contained alkaloids, flavonoids, tannins, and saponins. However, the screening was qualitative in nature and did not determine the concentration of each compound. Based on these findings, the extract was formulated into a mucoadhesive patch and subsequently subjected to physicochemical evaluation. The physicochemical properties evaluated included weight uniformity, thickness uniformity, folding endurance, surface pH, and mucoadhesive strength. The results are presented in Table 2.

Table 2. Physicochemical Properties of the Mucoadhesive Patch

Physical Properties Test of Patch	**Treatment Group (P)**	**Negative Control (K−)**
Weight uniformity	0,02 g	0,02 g
Thickness uniformity	1 mm	0,5 mm
Folding endurance	>350 folds	>300 folds
Surface pH	6,86	7,31
Mucoadhesive strength	1 h 55 s	30 m 22 s

Traumatic ulcers were induced on the labial mucosa of Wistar rats using a 2-mm biopsy punch. The mucoadhesive patch was applied twice daily, and ulcer diameter was measured on days 1, 3, 5, 7, and 10 at 4:00 p.m. using a digital sliding caliper.



(A) (B)

Figure 1. (A) Traumatic ulcer induced on the labial mucosa of a Wistar rat. (B) Application of the mucoadhesive patch to the traumatic ulcer on the labial mucosa.

Based on the observations, the mean ulcer diameter and standard deviation measured on days 1, 3, 5, 7, and 10 are presented in Table 3 and Figure 2.

Table 3. Mean ± Standard Deviation of Traumatic Ulcer Diameter (mm) on the Labial Mucosa of Wistar Rats

Day	Group		
	K+	P	K-
1	2.04 ± 0.35	3.26 ± 0.35	3.53 ± 0.86
3	2.03 ± 0.26	3.03 ± 0.35	3.40 ± 0.67
5	1.92 ± 0.27	2.82 ± 0.35	3.34 ± 0.66
7	1.56 ± 0.28	1.75 ± 0.16	3.20 ± 0.65
10	0	0	1.57 ± 0.08

Note:
K+: Positive control group treated with Aloclair® gel.
P: Mucoadhesive patch containing 35% *Cinnamomum burmannii* leaf extract formulated with HPMC and Carbopol® 940P.
K−: Negative control group treated with a placebo mucoadhesive patch.

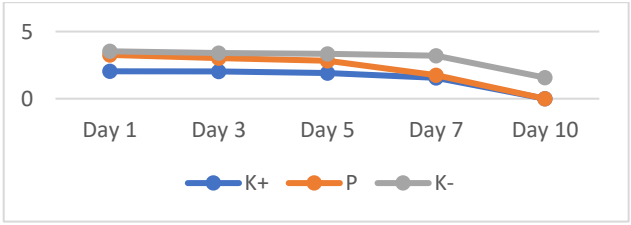


Figure 2. Changes in the diameter of traumatic ulcers on the labial mucosa of Wistar rats during the observation period.

The ulcer diameter data were first analyzed using the Shapiro–Wilk normality test. On days 1, 3, 5, and 7, all groups showed p-values > 0.05, indicating that the data were normally distributed and met the assumptions for parametric analysis. On day 10, both the positive control (K+) and treatment (P) groups exhibited complete ulcer healing, resulting in an ulcer diameter of zero (variance = 0). Consequently, the data were no longer normally distributed, making homogeneity testing and parametric analysis inappropriate. Therefore, the day-10 data were analyzed descriptively and demonstrated that both the positive control and treatment groups achieved complete ulcer healing, whereas ulcers remained present in the negative control group.

Homogeneity of variance was subsequently assessed using Levene's test. On days 1, 3, 5, and 7, all groups showed p-values > 0.05, indicating homogeneous variances. Accordingly, the data met the assumptions for one-way analysis of variance (ANOVA).

Table 4. Summary of One-Way ANOVA Results for Traumatic Ulcer Diameter

Observation Day	**Group**	**p-value**
Day 1	K+ P	0,001

Day 3	K-	
	K+	
	P	0,000
Day 5	K-	
	K+	
	P	0,000
Day 7	K-	
	K+	
	P	0,000
	K-	

Note: Statistical significance was set at **p < 0.05**.

One-way ANOVA was performed on days 1, 3, 5, and 7 using a 95% confidence level. The analysis demonstrated statistically significant differences among the three experimental groups at each observation time ($p < 0.05$), indicating that the treatments produced significantly different effects on the healing of traumatic ulcers in Wistar rats. To identify which groups differed significantly, Bonferroni's post hoc test was subsequently performed.

Table 5. Bonferroni Post Hoc Analysis of Traumatic Ulcer Diameter

Day	Group	Compare	Mean Difference	Sig
1	K+	P	-1,22	0,006*
		K-	-1,48	0,001*
	P	K+	1,22	0,006*
		K-	-0,26	1.000
	K-	K+	1,48	0,001*
		P	-0,26	1,000
3	K+	P	-1,00	0,006*
		K-	-1,37	0,000*
	P	K+	1,00	0,006*
		K-	-0,37	0,562
	K-	K+	1,37	0,000*
		P	0,37	0,562
5	K+	P	-0,89	0,014*
		K-	-1,42	0,000*
	P	K+	0,89	0,014*
		K-	-0.52	0,209
	K-	K+	1,42	0,000*
		P	0,52	0,209
7	K+	P	-0,18	1,000
		K-	-1,64	0,000*
	P	K+	0.18	1,000
		K-	-1,45	0,000*
	K-	K+	1,64	0,000*
		P	1,45	0,000*

Note: *Statistically significant at **p < 0.05**.*

The Bonferroni post hoc analysis revealed that, on days 1, 3, and 5, no significant difference was observed between the treatment group (P) and the negative control group (K−) ($p > 0.05$). In contrast, significant differences were found between the positive control group (K+) and the negative control group (K−), as well as between the positive control group (K+) and the treatment group (P) ($p < 0.05$).

By day 7, the treatment group (P) showed a statistically significant difference compared with the negative control group (K−) ($p < 0.05$), while no significant difference was observed between the treatment group (P) and the positive control group (K+) ($p > 0.05$). A significant difference remained between the positive control group (K+) and the negative control group (K−).

Overall, these findings indicate that the mucoadhesive patch containing *Cinnamomum burmannii* leaf extract began to exhibit a significant therapeutic effect by day 7, achieving healing outcomes comparable to those of the positive control while demonstrating superior efficacy compared with the placebo-treated group.

DISCUSSION

Traumatic ulcer is an ulcerative lesion of the oral mucosa caused by chemical or mechanical trauma, such as friction from orthodontic appliances, consumption of hard or hot foods, or accidental biting of the oral tissues. Clinically, traumatic ulcers are characterized by a whitish-yellow ulcer base covered with a fibrinous pseudomembrane, surrounded by an erythematous halo, and accompanied by pain upon palpation. These clinical features reflect ongoing vasodilation, inflammatory cell infiltration, and epithelial tissue damage1. During clinical examination, the erythematous border surrounding the ulcer provides the clearest margin for determining lesion size. Therefore, ulcer diameter was measured from one erythematous edge to the opposite edge as an

objective parameter for evaluating wound healing progression[12,13].

The present study demonstrated that, on day 1, the ulcer diameter in the treatment group (P) was comparable to that in the negative control group (K−), resulting in no statistically significant difference in the post hoc analysis. This finding may be attributed to the anti-inflammatory activity of flavonoids, which had not yet reached its optimal effect in suppressing inflammatory mediators during the early stage of wound healing; consequently, tissue repair remained minimal. On day 3, signs of healing became evident in the treatment group; however, no significant difference was observed compared with the negative control because the inflammatory phase was still ongoing and the proliferative phase had only recently begun. This observation is consistent with the wound healing process, in which fibroblasts surrounding the wound are initially stimulated to proliferate, resulting in limited granulation tissue formation. By day 5, ulcer diameter in the treatment group had decreased more noticeably than on day 3, although the difference remained statistically insignificant compared with the negative control. At this stage, fibroblasts had actively migrated and proliferated within the wound area, leading to progressive granulation tissue formation and gradual closure of the ulcer margin[13].

On days 1, 3, and 5, the positive control group (K+) consistently exhibited significantly smaller ulcer diameters than both the treatment group (P) and the negative control group (K−). This outcome is likely attributable to the presence of polyvinylpyrrolidone (PVP) in Aloclair® gel, which acts as a mucoprotective agent by forming a protective barrier over the ulcer surface. In addition, hyaluronic acid and Aloe vera contained in the formulation facilitate the natural wound healing process[14]. By day 7, the treatment group showed a statistically significant improvement compared with the negative control but did not differ significantly from the positive control, indicating that the therapeutic efficacy of the *Cinnamomum burmannii* mucoadhesive patch approached that of Aloclair® gel. At this stage, fibroblasts reached their peak population and became the predominant cells involved in tissue repair, resulting in thicker and denser granulation tissue. Furthermore, the anti-inflammatory activity of flavonoids, the astringent effect of tannins in reducing wound exudate, and the ability of saponins to stimulate fibroblast activity likely acted synergistically to accelerate wound healing. These effects were further enhanced by the prolonged adhesion time of the mucoadhesive patch, which enabled sustained release of the active compounds at the application site[10,15].

Mucoadhesive patches are capable of maintaining drug bioavailability by prolonging the contact time and residence time of the formulation at the site of application, thereby reducing dosing frequency and improving patient compliance[16]. The mucoadhesive layer firmly adheres to the oral mucosa and regulates the controlled release of the active compounds. Drug release and penetration are influenced by both the physicochemical properties of the active ingredient and the composition of the polymeric matrix[17].

Compared with conventional dosage forms, mucoadhesive patches are non-invasive, produce minimal adverse effects, and maintain drug bioavailability through strong adhesion to the oral mucosa. Moreover, this delivery system bypasses first-pass metabolism, thereby enhancing drug effectiveness while minimizing degradation within the gastrointestinal tract. Mucoadhesive patches are also convenient to use, and treatment can be discontinued immediately by removing the patch if adverse reactions or dosing errors occur, thereby reducing the risk of more serious complications[11,18].

The therapeutic effect of the mucoadhesive patch is closely associated with the physiological stages of wound healing. During the inflammatory phase, the patch maintains a moist wound environment and provides protection against microbial contamination, thereby supporting macrophage activity and the release of growth factors, including transforming growth factor-beta (TGF-β), transforming growth factor-alpha (TGF-α), fibroblast growth factor (FGF), and vascular endothelial growth factor (VEGF). During the proliferative phase, the sustained release of active compounds promotes epithelial cell migration and proliferation while stimulating myofibroblast activation, thereby accelerating granulation tissue formation and re-epithelialization. In addition, the patch maintains an optimal wound environment that supports angiogenesis. During the remodeling phase, the patch facilitates fibroblast differentiation into myofibroblasts, promotes collagen reorganization, and enhances the tensile strength of the newly formed tissue. Collectively, these mechanisms not only accelerate wound healing but also improve the quality of the regenerated tissue[19].

The findings of the present study demonstrated that the mucoadhesive patch containing 35% *Cinnamomum burmannii* leaf extract produced a significant therapeutic effect, with healing efficacy comparable to that of Aloclair® gel, the current standard therapy. The observed therapeutic effect is likely attributable to the synergistic activity of the bioactive compounds present in cinnamon leaf extract, which accelerate the early inflammatory response, promote tissue proliferation, and enhance re-epithelialization. Therefore, the *Cinnamomum burmannii* mucoadhesive patch represents a promising natural alternative for the treatment of traumatic ulcers.

CONCLUSSION

The findings of this study demonstrate that a mucoadhesive patch containing *Cinnamomum burmannii* leaf extract effectively reduced the diameter of traumatic ulcers in Wistar rats (Rattus norvegicus), indicating its potential as a natural alternative therapy for the management of traumatic ulcers. Considering the limitations of this study, future research is recommended to perform quantitative phytochemical analyses, such as High-Performance Liquid Chromatography (HPLC), to to determine the concentration and profile of the bioactive compounds in *Cinnamomum burmannii* leaf extract. In addition, histopathological evaluations, including fibroblast count, collagen density, and epithelial thickness, are recommended to provide a more comprehensive understanding of the wound-healing mechanism. The use of standardized calibrated photographic documentation and assessments by multiple independent observers is also recommended to reduce measurement bias and enhance the validity and reliability of the findings.

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