

ENHANCING INCISED WOUND HEALING IN MICE USING GARCINIA MANGOSTANA STEM BARK AND PERICARP EXTRACTS

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Abstract. Wounds are tissue injuries caused by various external and internal factors that may disrupt the normal function of the affected tissue. Numerous studies have focused on the use of natural substances as complementary therapies to accelerate wound healing. One plant that has demonstrated therapeutic potential is *Garcinia mangostana* L. This study aimed to evaluate the therapeutic potential of stem bark and pericarp extracts of *Garcinia mangostana* L. in accelerating the healing of incised wounds in mice (*Mus musculus*). A Completely Randomized Design (CRD) was employed, consisting of six treatment groups with three replicates each: negative control (K⁻), positive control (K⁺), and mice treated with combined extracts of stem bark and pericarp of *G. mangostana* at concentrations of 25%, 50%, 75%, and 100%. All mice were inflicted with an incised wound measuring 1 cm in diameter. The wound healing process was observed over 13 days, with measurements taken every three days. The results showed that administration of the extracts significantly accelerated the healing of incised wounds in mice. These findings suggest that *Garcinia mangostana* L. has potential as a complementary therapy to enhance wound healing, providing a basis for further studies on its application in humans.

Keywords: *Garcinia mangostana* L., stem bark, pericarp, wound healing, incised wound

Introduction

A wound is a condition in which body tissue is damaged due to various factors, such as sharp objects, chemicals, animal bites, or electric shock. There are different types of wounds, classified based on their causes (Mlambo et al, 2022; Kirwan and Pignataro, 2015). For instance, an incised wound (*vulnus scissum*) is caused by sharp objects, while a puncture wound (*vulnus punctum*) results from pointed objects (Fatmawati et al., 2020). A lacerated wound (*vulnus laceratum*) typically has irregular edges due to rough-surfaced objects (Tafor et al., 2019), whereas an abrasion (*vulnus excoriatum*) occurs due to friction (Susanti et al., 2022). Burn wounds (*vulnus combustion*) are caused by heat or chemical agents (Williams and Lee, 2018). An incised wound is a type of tissue injury caused by sharp objects that may result in bleeding and initiate hemostatic mechanisms, followed by inflammation (Upadhyay et al., 2021; Visha and Karunakaran, 2019). In the early inflammatory phase, as well as during the proliferative and remodeling stages, vasoconstriction occurs to stop bleeding, restore blood flow, and facilitate the inflammatory response. This process plays a critical role in removing damaged tissue and preventing bacterial infection (Abdulkhaleq et al., 2018). According to Honnegowda et al. (2015), wound healing involves several key components, including collagen, angiogenesis, and granulation tissue formation. Collagen serves as a structural matrix that supports tissue regeneration (Ferreira et al., 2012). Angiogenesis is crucial for the formation of new blood vessels to deliver oxygen and nutrients to the wound site (DiPietro, 2016). Granulation involves the growth of new connective tissue and blood vessels, which are essential for wound closure. These components work synergistically to accelerate healing and restore tissue integrity.

Proper wound management is essential to accelerating the healing process (Kolimi et al., 2022). As noted by Murwaningsih and Waluyo (2021), appropriate treatment can prevent infection, reduce inflammation, and promote faster tissue regeneration. Wound care includes cleansing to remove debris and bacteria, applying antiseptics to prevent disease, and covering the wound to protect it from external factors. Additionally, natural substances can stimulate collagen production, improve blood circulation, and enhance granulation, thus promoting faster healing. Indonesia is rich in traditional medicinal resources, widely used by local communities across generations (Handayani et al., 2001). One of the advantages of traditional medicinal plants is their accessibility and the ability to grow them at home (Karunamoorthi et al., 2013). Among these is the mangosteen (*Garcinia mangostana* L.), which is commonly used to treat various ailments (Ansori et al., 2020). Mangosteen (*Garcinia mangostana* L.) is a tropical plant known for its sweet and tangy fruit (Kaur et al., 2020). The fruit has a thick purple rind and white flesh and is rich in vitamin C, antioxidants, and other bioactive compounds beneficial to human health. In addition to the edible portion, different parts of the plant, including the pericarp and stem bark, are known to contain active compounds traditionally used for medicinal purposes. In *G. mangostana*, the rind comprises approximately 70-75% of the fruit, while the pulp accounts for 10-15%, and the seed 15-20%. The rind contains xanthones, flavonoids, anthocyanins, and tannins (Yuvanatemiya et al., 2022). Xanthones have been reported to reduce inflammation around wounds, a common barrier to healing (Gunter et al., 2020). According to Hossain et al. (2021), tannins function as astringents by forming protein layers on cell surfaces with low permeability, which constrict pores, reduce leakage and bleeding and promote wound closure. Tannins also help prevent exudate and minor hemorrhage, contributing to wound sealing and hemostasis (Montazerian et al., 2020). This study aims to evaluate the therapeutic potential of stem bark and pericarp extracts of *Garcinia mangostana* L. in accelerating the healing of incised wounds in mice (*Mus musculus*).

Materials and Methods

This study employed a post-test-only design using a Completely Randomized Design (CRD). The tools used included a caliper (Krisbow), analytical balance (Ohaus), animal cages, 500 mL beakers (Iwaki), porcelain dishes, and a rotary evaporator (IKA). Materials included male mice, distilled water, *G. mangostana* pericarp and stem bark, petroleum ether, ketamine, filter paper, and 10% povidone-iodine ointment®. Fresh (wet) samples of *G. mangostana* stem bark and pericarp were washed, chopped into small pieces, air-dried for two weeks, ground using a blender, and sieved through a 65-mesh sieve to obtain fine powder. A total of 50 grams of *G. mangostana* stem bark, and pericarp powder was macerated in 200 mL of petroleum ether for 24 hours with periodic stirring. The mixture was filtered using vacuum filtration and filter paper to separate the residue from the filtrate. The filtrate was then evaporated to remove the solvent. The resulting thick extract was weighed and stored at 40°C (Kaihena et al., 2024a; Ukratalo et al., 2022). Fifteen male mice were divided into six groups: a negative control group (K-), a positive control group treated with povidone-iodine ointment (K+), and four treatment groups administered stem bark and pericarp extracts of *G. mangostana* at concentrations of 25% (P1), 50% (P2), 75% (P3), and 100% (P4). Prior to the experiment, the mice were acclimatized for two weeks and fed a standard diet. On the first day, the dorsal fur was shaved, and a 1 cm incised wound was created under

intraperitoneal ketamine anesthesia. The wound-healing process was observed over 13 days, and measurements were taken every three days.

The percentage of incised wound healing was calculated using the formula proposed by Megawati and Kurniasih (2020):

$$\% \text{ Wound Healing} = \frac{\text{Healed Area}}{\text{Initial Wound Length}} \times 100\% \quad \text{Eq. (1)}$$

The healed area refers to the reduction in wound length, calculated by subtracting the remaining wound length from the initial wound length (Milasanti et al., 2023). The collected data were analyzed using Analysis of Variance (ANOVA) with SPSS version 24.00. If significant differences were detected, the analysis was followed by a Least Significant Difference (LSD) test at a significance level of 0.05 (Kaihen et al., 2024b; Ukratalo et al., 2023).

Results and Discussion

Table 1 and *Table 2* present the results of wound diameter measurements in the negative control group, positive control group (treated with Lanakeloid ointment), and treatment groups receiving incised wounds followed by therapy with combined stem bark and pericarp extracts of *Garcinia mangostana*. As shown in *Table 1*, in the negative control group (K−), the incised wound diameter increased from 1.0 cm to 1.63 cm by day 13. In contrast, the positive control group (K+) demonstrated optimal wound healing, with the wound diameter reduced to only 0.01 cm. The groups treated with *G. mangostana* pericarp extract at concentrations of 25%, 50%, 75%, and 100% also exhibited progressive reductions in wound diameter by day 13, reaching 0.61 cm, 0.42 cm, 0.27 cm, and 0.10 cm, respectively. Observations in *Table 2* revealed a similar pattern for the treatment with stem bark extract. In the negative control group (K−), the wound diameter increased from 1.0 cm on day 0 to 1.65 cm by day 13. Conversely, the positive control group (K+) exhibited rapid wound closure, with the wound diameter reduced to 0.06 cm on day 13. The groups treated with *G. mangostana* stem bark extract at concentrations of 25%, 50%, 75%, and 100% showed reductions in wound diameter to 0.78 cm, 0.55 cm, 0.49 cm, and 0.19 cm, respectively. These findings indicate that both pericarp and stem bark extracts of *Garcinia mangostana* were effective in accelerating incised wound healing. However, the healing rate remained slower than that observed in the positive control group.

Table 1. Mean diameter of incised wounds in mice treated with *G. mangostana* Pericarp Extract.

Treatment	Mean incised wound diameter (cm)					Mean ± SD
	Day 0	Day 4	Day 7	Day 10	Day 13	
Negative Control	1,0	1,27	1,30	1,50	1,63	1,34 ± 0,19 ^a
Positive Control	1,0	0,83	0,65	0,34	0,01	0,57 ± 0,44 ^b
25% Concentration	1,0	0,98	0,89	0,80	0,61	0,87 ± 0,27 ^c
50% Concentration	1,0	0,96	0,84	0,77	0,42	0,79 ± 0,32 ^d
75% Concentration	1,0	0,93	0,83	0,70	0,27	0,74 ± 0,37 ^e
100% Concentration	1,0	0,88	0,75	0,46	0,10	0,63 ± 0,44 ^f

Note: Superscripts with the same letter are not significantly different ($\alpha = 0.05$).

Table 2. Mean diameter of incised wounds in mice treated with *G. mangostana* Stem Bark Extract.

Treatment	Mean incised wound diameter (cm)					Mean $\pm$ SD
	Day 0	Day 4	Day 0	Day 10	Day 0	
Negative Control	1,0	1,28	1,30	1,57	1,65	1,36 $\pm$ 0,22 ^a
Positive Control	1,0	0,88	0,70	0,41	0,06	0,61 $\pm$ 0,44 ^b
25% Concentration	1,0	0,96	0,91	0,85	0,78	0,99 $\pm$ 0,29 ^c
50% Concentration	1,0	0,96	0,88	0,79	0,55	0,84 $\pm$ 0,30 ^d
75% Concentration	1,0	0,94	0,87	0,73	0,49	0,81 $\pm$ 0,38 ^e
100% Concentration	1,0	0,91	0,80	0,51	0,19	0,68 $\pm$ 0,44 ^b

Note: Superscripts with the same letter are not significantly different ($\alpha = 0.05$).

ANOVA results confirmed that the administration of both pericarp and stem bark extracts of *G. mangostana* had a statistically significant effect on wound healing in mice ($p < 0.05$). The detailed statistical outcomes are presented in *Table 3* and *Table 4*. The Least Significant Difference (LSD) test further revealed that there were statistically significant differences among the negative control, the positive control, and the treatment groups that received *G. mangostana* pericarp and stem bark extracts at concentrations of 25%, 50%, 75%, and 100%. The percentage of wound healing, calculated using the data in *Table 1* and *Table 2*, is presented in *Table 5*. As shown in *Table 5*, the negative control group (K⁻) experienced a substantial decrease in wound healing percentage, with values of -63% for the pericarp extract and -65% for the stem bark extract. These results indicate a lack of healing progress in untreated wounds. In contrast, the positive control group (K⁺) demonstrated excellent healing outcomes, achieving wound healing percentages of 99% for the pericarp extract and 94% for the stem bark extract. Among the treatment groups (P1 to P4), pericarp extract consistently showed higher wound healing percentages than stem bark extract. Specifically, the pericarp extract at concentrations of 25%, 50%, 75%, and 100% resulted in healing percentages of 39%, 58%, 73%, and 90%, respectively. Meanwhile, the stem bark extract at the same concentrations yielded healing percentages of 22%, 45%, 51%, and 81%, respectively. These findings further support the potential therapeutic role of *Garcinia mangostana* extracts in accelerating wound healing, with the pericarp extract demonstrating slightly greater efficacy than the stem bark extract.

Table 3. ANOVA results of the effect of Mangosteen (*G. mangostana*) Pericarp Extract on wound healing in mice.

Source	Type III sum of squares	df	Mean square	F	Sig.
Corrected Model	13.262 ^a	29	.457	79.152	.000
Intercept	73.441	1	73.441	12710.942	.000
Treatment	3.252	5	.650	112.558	.000
Time Interval (Measurement Time)	6.631	4	1.658	286.904	.000
Treatment * Time	3.380	20	.169	29.250	.000
Error	.347	60	.006		
Total	87.050	90			
Corrected Total	13.609	89			

Note: a. R squared = .975 (Adjusted R squared = .962); Dependent variable = Mice wound diameter.

Table 4. ANOVA results of the effect of Mangosteen (*G. mangostana*) Stem Bark Extract on wound healing in mice.

Source	Type III sum of squares	df	Mean square	F	Sig.
Corrected Model	13.509 ^a	29	.466	66.546	.000
Intercept	74.711	1	74.711	10673.016	.000
Treatment	3.162	5	.632	90.349	.000
Time Interval (Measurement Time)	6.692	4	1.673	239.008	.000
Treatment * Time	3.654	20	.183	26.103	.000
Error	.420	60	.007		
Total	88.640	90			
Corrected Total	13.929	89			

Note: *a. R squared = .970 (Adjusted R squared = .955); Dependent variable = Mice wound diameter.*

Table 5. *Percentage of incised wound healing in mice.*

Treatment	Pericap extract (%)	Stem bark extract (%)
Negative Control	-63	-65
Positive Control	99	94
25% Concentration	39	22
50% Concentration	58	45
75% Concentration	73	51
100% Concentration	90	81

Wound healing is a complex process involving tissue function restoration and the recovery of the anatomical continuity of the body after injury (Sorg et al., 2017). According to Landén et al. (2016), wound healing can be divided into three stages: the inflammatory, proliferative, and remodeling phases, which are part of the tissue repair process. The inflammatory phase lasts from the time of injury to about the fifth day and consists of vascular and cellular phases. The main goal of this phase is to stop bleeding, prevent infection, and remove damaged tissue, foreign bodies, and microorganisms (Miller, 2016). This phase, often referred to as the reactive phase, is the initial stage in the wound-healing process and lasts from the occurrence of the injury until around day five (Hosgood 2006). The proliferative phase lasts from day 3 to day 24 and is marked by the formation of new blood vessels as part of the reconstruction process. Once the formation of granulation tissue covers the wound surface, the fibroplasia process ceases and is followed by the maturation of tissue in the remodeling phase. During this regenerative phase, the main activity is to fill the wound with new connective or granulation tissue and to close the wound surface with healing. A wound is considered healed when it is closed, dry, and free from redness, discharge, swelling, and signs of allergic reactions around the wound. On the first day after the incision, bleeding was observed on the backs of several mice due to the cutting of blood vessels, likely involving vessels in the papillary layer (Hess, 2012). Physiologically, the body initiates the coagulation cascade to stop the bleeding and begin the hemostasis process. This process is controlled by vasospasm, which leads to the constriction of blood vessels (Periayah et al., 2017).

According to Strodbeck (2001), the maturation process in wound healing requires a relatively long time and is heavily influenced by the depth and extent of the wound. In the negative control group (K-) of this study, no significant improvement was observed in the incised wounds. This was evident from the increasing size of the wound over time, suggesting that the healing process in this group was disturbed or did not proceed well. This condition indicates that, without appropriate intervention or treatment, wound healing can take longer or may not show any signs of improvement at all. The positive control group treated with 10% povidone-iodine ointment showed nearly 100% wound healing on average. Povidone iodine is an antiseptic commonly used for wound care, helping to maintain wound cleanliness and reduce the likelihood of bacterial contamination that could lead to infection (Bigliardi et al., 2017). Several factors that support the wound healing process include personal hygiene, immune system function, blood distribution carrying oxygen to the wound area, and the wound condition itself. Based on the ANOVA analysis, the administration of *G. mangostana* fruit peel and stem bark extracts significantly accelerated incised wound healing in mice. The study results

showed that the fruit peel extract of *G. mangostana* had a better capacity to accelerate wound healing, achieving a healing percentage of 90%. Meanwhile, the stem bark extract also showed significant results, with a healing rate of 81%. Both extracts demonstrated remarkable potential in stimulating the wound healing process, although the fruit peel extract provided more optimal results. One factor underlying the effectiveness of *G. mangostana* fruit peel and stem bark extracts in wound healing is the presence of bioactive compounds, such as xanthenes, in both plant parts. Xanthenes, predominantly found in the fruit peel of *G. mangostana*, are known for their anti-inflammatory, antibacterial, and antioxidant properties, which help reduce inflammation and prevent infection in wounds. Xanthenes also play a role in stimulating collagen production, which is crucial for the formation of new tissue during the healing process (Patrick et al., 2024). These compounds assist in accelerating tissue regeneration and improving the integrity of the skin damaged by incised wounds.

In addition to xanthenes, the stem bark of *G. mangostana* contains various bioactive compounds, including flavonoids and tannins, which have the potential to accelerate wound healing. According to Al-Khayri et al. (2022), flavonoids play an essential role in the inflammatory, proliferative, and remodeling phases. Flavonoids act as antibacterial agents by denaturing proteins, which results in the cessation of metabolic activity and bacterial cell death. Flavonoids also have anti-inflammatory effects by inhibiting cyclooxygenase and lipoxygenase enzymes (Hanáková et al., 2017). Furthermore, flavonoids act as antioxidants that can inhibit and stop free radical reactions, preventing tissue damage by disrupting the free radical chain reaction. Flavonoids can also stabilize reactive oxygen species (ROS) produced by neutrophils and macrophages, preventing them from attacking cells, inhibiting angiogenesis, and enhancing epithelial cell proliferation and collagen production (Zulkefli et al., 2023). With their functions as anti-inflammatory and antioxidant agents, flavonoids can accelerate wound healing by shortening the duration of inflammation. Tannins play roles in the inflammatory, proliferative, and remodeling phases (Pattarayan et al., 2018). Tannins possess antimicrobial properties that can enhance healing and contribute to wound contraction (Li et al., 2011). In addition, tannins function as anti-inflammatory agents by speeding up the neutrophil and macrophage responses and stimulating phagocytosis formation in the body. As antibacterials, tannins can damage the peptidoglycan structure of bacterial cell walls, causing cell instability and ultimately leading to bacterial cell death.

Conclusion

Garcinia mangostana fruit peel and stem bark extracts can accelerate the healing process of incised wounds in mice. This is attributed to the bioactive compounds present in both plant parts, such as xanthenes, flavonoids, and tannins. The combination of these compounds supports a faster and more efficient wound healing process, making *Garcinia mangostana* fruit peel and stem bark extracts a promising alternative for wound treatment.

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Conflict of interest

The authors confirm that there is no conflict of interest involve with any parties in this research study.

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