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ORIGINAL RESEARCH

THE EFFECT OF TOPICAL A-MANGOSTIN DERIVED FROM MANGOSTEEN PEEL (GARCINIA MANGOSTANA LINN) ON THE HEALING OF ACUTE FULL-THICKNESS WOUNDS IN RATS (RATTUS NORVEGICUS)

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ABSTRACT

Background: Wound healing is a complex biological process involving three main phases: inflammation, proliferation, and tissue remodeling. Full-thickness wounds, which extend through the entire skin layer down to the subcutaneous tissue, require effective therapeutic interventions to accelerate regeneration. Garcinia mangostana peel extract, particularly its active compound α-mangostin, has demonstrated antioxidant, anti-inflammatory, and antimicrobial properties. However, in vivo evidence regarding its topical effect on specific wound healing parameters remains limited.

Methods: This laboratory-based experimental study used a randomized post-test only control group design with 16 male Wistar rats (12 weeks, 180–200 g) divided into four groups: control day-5, control day-10, treatment day-5, and treatment day-10. A 2×2 cm full-thickness wound was created dorsally under ketamine anesthesia. Treatment groups received 1% α-mangostin topical gel formulated from >90% purified extract. Wound tissues were collected on days 5 and 10 for histopathological evaluation. Healing was assessed through epithelial thickness, angiogenesis, and collagen density using hematoxylin-eosin (HE) and Masson's Trichrome (MT) staining. Statistical analysis was performed using SPSS v27 (Shapiro-Wilk, independent t-test, and Mann-Whitney; $p < 0.05$ considered significant).

Results: On day 10, the treatment group showed significantly higher epithelial thickness ($p = 0.019$), angiogenesis ($p = 0.017$), and collagen density ($p = 0.004$) than controls. On day 5, angiogenesis ($p = 0.017$) and collagen density ($p = 0.027$) were also significantly improved, while epithelialization was not yet significant ($p = 0.098$).

Conclusion: Topical α-mangostin significantly enhances full-thickness wound healing by promoting early angiogenesis and collagen formation, followed by improved epithelial regeneration. It shows promise as a phytopharmaceutical candidate for wound therapy.

Keywords: α-mangostin; Garcinia mangostana; full-thickness wound; wound healing

INTRODUCTION

Full-thickness skin wounds, defined as injuries that extend through the entire dermis into the subcutaneous layer, remain a major clinical challenge. They are prone to infection, prolonged pain, delayed re-epithelialization and excessive scarring, all of which impair function and appearance and inflate healthcare costs.[1,2] Because wound repair is a tightly orchestrated sequence of inflammation, proliferation and remodeling, disruption of any phase can halt healing and lower quality of life for patients.[3,4]

Standard management in plastic and reconstructive surgery ranges from secondary intention healing and primary closure to skin grafting, commercial skin substitutes, negative-pressure wound therapy and topical growth factors.[5] Although these approaches shorten closure time, they are expensive, not universally available and may provoke immunological rejection or recurrent infection. These constraints have driven the search for complementary, safer and more affordable wound therapies.[6]

Mangosteen peel (Garcinia mangostana Linn) has gained attention because it is rich in xanthones, with α-mangostin being the most abundant. In vitro, α-mangostin exhibits strong antioxidant, anti-inflammatory and broad-spectrum antimicrobial activities, notably against Staphylococcus aureus and Staphylococcus epidermidis.[7-9] Crude peel extracts down-regulate pro-inflammatory mediators such as COX-2, IL-6, IL-1β and nitric oxide, suggesting that they could temper the inflammatory phase of wound healing.[10] Because the compound is plant-derived, advocates argue that it offers good biocompatibility and lower systemic toxicity than many synthetic agents.[11]

The present study therefore aims to evaluate the effect of a well-characterized topical α-mangostin preparation, isolated from mangosteen peel, on the healing of acute full-thickness excisional wounds in rats (Rattus norvegicus). By monitoring macroscopic closure, histological parameters and inflammatory markers, we aimed to investigate whether α-mangostin accelerates and improves tissue repair compared with a standard ointment base. The findings support the compound's potential as a cost-effective adjunct for full-thickness wound management.

MATERIALS AND METHODS

Study design and animals

This laboratory experiment followed a randomized post-test only control group design. Sixteen male Wistar rats (Rattus norvegicus), 12 weeks old, 180–200 g, were housed six per polypropylene cage (30 × 40 × 15 cm) at 32 °C with free ventilation, PAR-G pellets (20 g day^{-1}) and water ad libitum. The minimum sample size of 16 animals was derived with the resource-equation method described in previous study.[12] After 7 days of acclimatization, rats were assigned by computer-generated random numbers to four groups (n = 4 each): control day-5 (C-5), control day-10 (C-10), treatment by α-mangostin day-5 (T-5) and treatment by α-mangostin day-10 (T-10). All procedures complied with the Guide for the Care and Use of Laboratory Animals and were approved by the Airlangga University Animal Care and Use Committee (No. 2.KEH.61.04.2025).

Topical α-mangostin formulation

Purified mangosteen-peel extract containing > 90 % α-mangostin (acquired from Andalas Sitawa Fitolab Co., Ltd., Indonesia) was dispersed in a carbopol hydrogel with propylene glycol, glycerin, triethanolamine, methyl paraben and sodium EDTA. α-Mangostin content was verified by high-performance liquid chromatography, and the gel was stored in opaque jars at 4 °C.

Surgical procedure and treatment protocol

Under intramuscular ketamine anesthesia (20 mg kg^{-1}), dorsal hair was clipped and disinfected with 10 % povidone-iodine followed by 1:30 Savlon. A single 2 × 2 cm full-thickness square wound was created with a sterile scalpel. Groups M-5 and T-10 received 0.1 g α-mangostin gel evenly spread over the wound; controls received no gel. All wounds were covered with a transparent semipermeable dressing and redressed twice daily at 08:00 and 18:00. On day 5 (C-5, T-5) or day 10 (C-10, T-10) rats were re-anaesthetized, the wound plus a 2 mm margin excised, and the animals euthanized by intraperitoneal pentobarbital (60–100 mg kg^{-1}). Specimens were fixed in 10 % neutral-buffered formalin.

Histological evaluation

Formalin-fixed tissues were embedded in paraffin, cut at 5 µm, and stained with both hematoxylin-eosin (HE) and Masson's trichrome (MT). A board-certified anatomical pathologist examined each slide with a Leica Flexacam i5 microscope at 400× magnification using Leica Enersight software v1.1.2. Five high-power fields per section were evaluated. Epithelial thickness and angiogenesis were graded 0–3 with the Gunawan scoring system, whereas collagen density was recorded as the raw percentage of MT-positive area in each field.[13]

Statistical analysis

Data were analyzed with SPSS v27. Normality was assessed by Shapiro–Wilk. Independent t-tests were applied to normally distributed data, meanwhile Mann–Whitney U-tests were used for abnormally distributed data. Significance was set at $p < 0.05$. Figures were prepared with GraphPad Prism v10.4.2.

RESULTS

All 16 rats completed the study without illness or mortality. Representative photographs of the 1 % α-mangostin hydrogel and surgical procedure are presented in Figure 1 and 2, respectively.

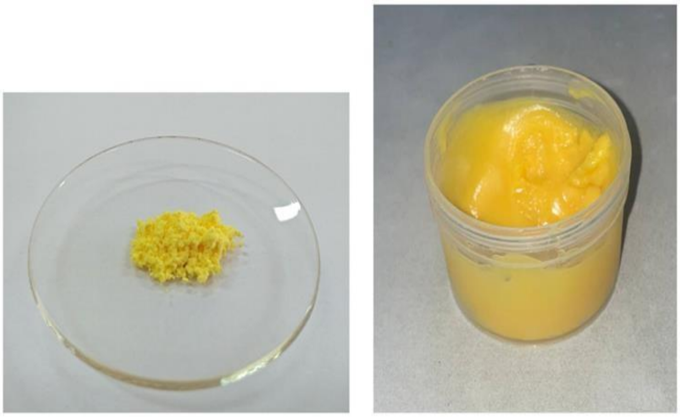

Figure 1. Purified α-mangostin powder (> 90 % purity) obtained from mangosteen peel (left) and the 1 % α-mangostin carbopol hydrogel formulated for topical application (right).

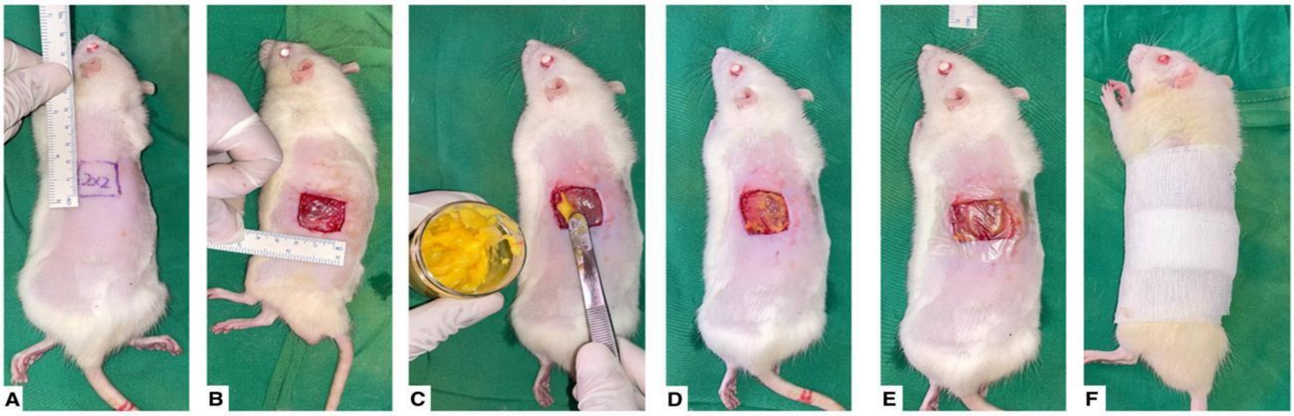

Figure 2. Step-by-step preparation of a 2 × 2 cm full-thickness dorsal wound in a Wistar rat: (a) shaving and marking the excision area, (b) creation of the wound, (c) topical application of 1 % α-mangostin hydrogel, (d) immediate wound appearance after treatment, (e) placement of a transparent semipermeable dressing, and (f) final bandaging.

Histological findings
Hematoxylin–eosin (HE) staining

By day 5, in the treated wounds a thin yet distinct epithelial layer was already present (green arrows). In the controls the epithelial rim was barely visible at the same magnification. Small new capillaries were common under the treated wounds (red arrows), while controls showed only a few such vessels and still contained many inflammatory cells and oedema. At day 10, re-epithelialization had occurred in both groups, but the epithelial layer was thicker and more orderly in the treated wounds. Capillaries were also more numerous and better formed than in the controls, where vessels were fewer and smaller (Figure 3).

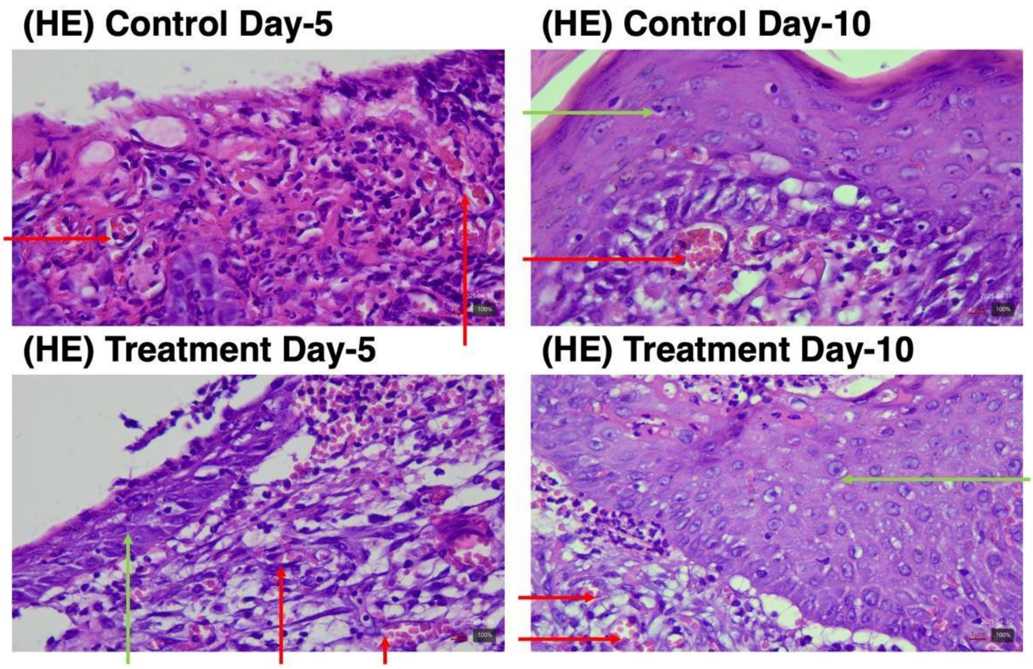

Figure 3. Representative hematoxylin–eosin (HE) micrographs of full-thickness wounds. Upper row: control groups on day 5 (left) and day 10 (right). Lower row: α-mangostin-treated groups on day 5 (left) and day 10 (right). Green arrows highlight the neo-epithelium; red arrows indicate newly formed blood vessels.

Masson's trichrome (MT) staining

By day 5, collagen in the control wounds appeared as faint, patchy blue areas with only a few thin bundles (white arrows). In the treatment group the blue signal was stronger and covered a wider area, showing that collagen deposition had begun earlier and was already denser than in controls. At day 10, treated wounds contained broad, compact, and mostly parallel collagen fibers that stained an intense blue. Control wounds still showed a light, uneven blue pattern with loosely organized fibers (Figure 4).

Burhan Husein, Iswinarno Doso Saputro, David Sontani Perdanakusuma, Hanif Ardiansyah Sulistya The Effect of Topical α-Mangostin Derived from Mangosteen Peel (Garcinia mangostana Linn) on the Healing of Acute Full-Thickness Wounds in Rats (Rattus norvegicus).Bulletin of Stomatology and Maxillofacial Surgery. Shetty2025;21(5).380-385 doi:10.58240/1829006X-2025.21.5-380

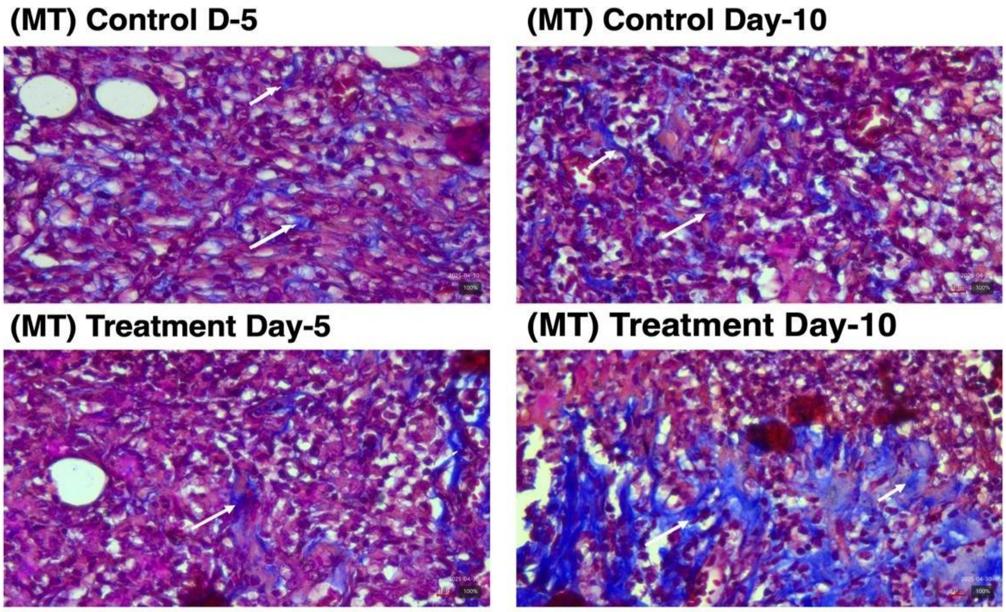

Figure 4. Masson's trichrome (MT) micrographs of full-thickness wounds. Upper row: controls on day 5 (left) and day 10 (right). Lower row: α-mangostin-treated wounds on day 5 (left) and day 10 (right). Blue staining marks collagen; white arrows highlight collagen bundles.

Statistical analysis

For epithelial thickness, the Mann–Whitney test detected a significant difference only between C-10 and T-10 ($p = 0.019$); C-5 vs T-5 and C-10 vs T-5 were non-significant ($p > 0.05$). An independent t-test showed that T-10 was also thicker than T-5 ($p = 0.002$). These findings indicate that the extract begins to increase epithelial thickness after day 5, with a clear effect by day 10. Angiogenesis followed a similar pattern. Mann–Whitney analysis showed higher vessel density in T-10 relative to C-10 ($p = 0.017$) and T-5 ($p = 0.036$), whereas C-5 vs C-10 was not significant ($p = 0.122$). The t-test confirmed that T-5 already exceeded C-5 ($p = 0.017$). Thus, the treatment enhances angiogenic activity from day 5 and this effect intensifies by day 10. Collagen density increased across all contrasts examined by t-test (all $p < 0.05$). Density rose over time in controls (C-5 vs C-10, $p = 0.017$) and was higher with treatment at each time-point (C-5 vs T-5, $p = 0.027$; C-10 vs T-10, $p = 0.004$). Within the treated group, T-10 also surpassed T-5 ($p = 0.021$). These results show that both wound age and topical α-mangostin additively promote collagen deposition (Table 1; Figure 5).

Table 1. Between-group analyses of each variables

Variable	Analysis between Groups		Group 1 Value	Group 2 Value	p-value
	Group 1	Group 2			
Epithelial thickness	Control Day-5†	Treatment Day-5†	0.2 (0.2)	0.3 (0.4)	0.098
	Control Day-10†	Treatment Day-5†	0.3 (0.2)	0.3 (0.4)	0.752
	Control Day-10†	Treatment Day-10†	0.3 (0.2)	0.1 (0.3)	0.019*
	Treatment Day-5‡	Treatment Day-10‡	0.35 ± 0.19	1.0 ± 0.16	0.002*
Angiogenesis	Control Day-5†	Treatment Day-10†	0.5 (0.5)	0.8 (0.2)	0.122
	Control Day-10†	Treatment Day-10†	0.8 (0.2)	1.3 (0.2)	0.017*
	Treatment Day-5†	Treatment Day-10†	1.0 (0.3)	1.3 (0.2)	0.036*
	Control Day-5‡	Treatment Day-5‡	0.5 ± 0.26	1.0 ± 0.16	0.017*
Collagen density	Control Day-5‡	Control Day-10‡	13.75 ± 8.54	28.75 ± 6.29	0.017*
	Control Day-5‡	Treatment Day-5‡	13.75 ± 8.54	32.50 ± 9.57	0.027*
	Control Day-10‡	Treatment Day-10‡	28.75 ± 6.29	52.50 ± 8.66	0.004*
	Treatment Day-5‡	Treatment Day-10‡	32.50 ± 9.57	52.50 ± 8.66	0.021*

*p-value significant at < 0.05, †Value displayed as median (IQR) and statistical analysis used Mann-Whitney test, ‡Value displayed as mean ± SD and statistical analysis used Independent t-test

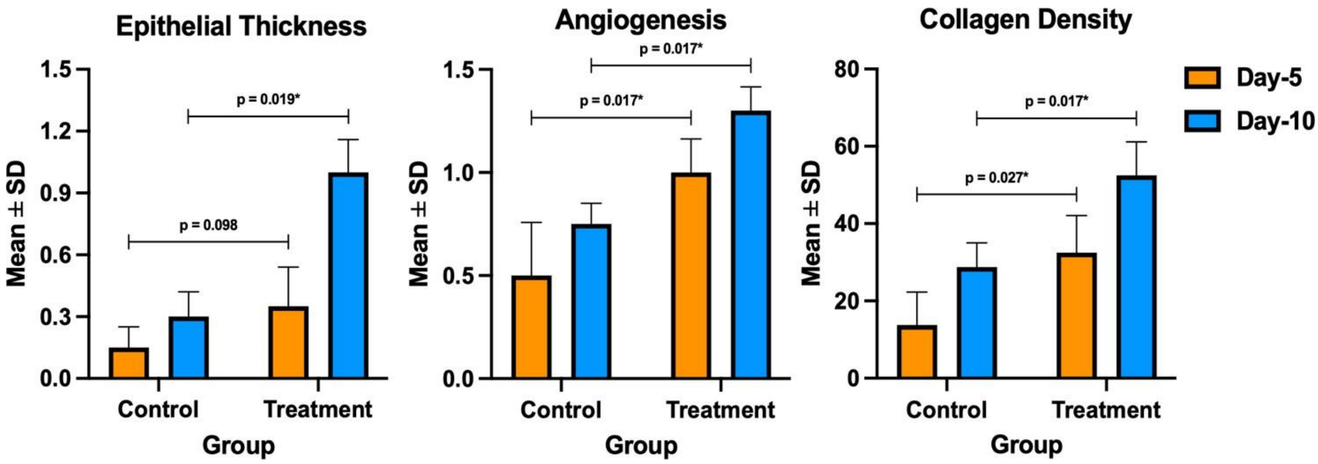

Figure 5. Comparative histograms illustrating epithelial thickness, angiogenesis score, and collagen density in control (C) and treatment (T) groups on day-5 (C-5, T-5) and day-10 (C-10, T-10).

DISCUSSION

This study demonstrates that topical application of α-mangostin (Garcinia mangostana Linn.) significantly enhances wound healing parameters in a full-thickness rat model, particularly by day 10. Three critical parameters, epithelialization, angiogenesis, and collagen density, all exhibited notable differences between the control and treatment groups by this time. On day 5, both angiogenesis and collagen density were significantly different, thus showcasing early effects of α-mangostin.[14]

The observed improvements align with the physiological phases of wound healing: inflammation, proliferation, and remodeling. Angiogenesis, crucially, supports the supply of oxygen and nutrients necessary for cellular activities such as fibroblast and keratinocyte migration and proliferation.[15] The early enhancement of angiogenesis on day 5 is considered a vital initiation that facilitates progression into re-epithelialization and extracellular matrix deposition. This modulation is likely attributed to the active compounds in mangosteen peel, especially α-mangostin, which is known for its potent antioxidant and anti-inflammatory effects.[16] The antioxidant properties help to mitigate local oxidative stress in the wound area, inhibit excessive inflammation, and enhance the release of angiogenic factors such as VEGF.[17]

Moreover, the significant increase in collagen density on both days 5 and 10 underscores collagen's essential role as a primary extracellular matrix component that provides tensile strength to the new tissue.[18] The data suggests that α-mangostin may stimulate fibroblast activation to produce collagen by modulating regenerative cytokines and growth factors. However, the specific molecular mechanisms need further investigation.

Interestingly, these findings differ slightly from a previous study which observed significant effects primarily on epithelialization using a 1% purified mangosteen extract.[7] The differences may stem from variations in topical formulation or the specific phyto-chemical composition in the non-purified extract. In addition, a supporting previous study corroborates that a 1% concentration of α-mangostin is optimal for promoting wound healing.[19]

The early significant effects on angiogenesis underscore its critical role as a trigger for the proliferative phase of healing. Enhanced vascularization ensures that healing cells receive an adequate supply of oxygen and growth factors necessary for effective recovery. Angiogenesis is essential for facilitating the subsequent processes of epithelialization and collagen remodelling, which are crucial for successful wound healing.[20]

In essence, this research reveals that α-mangostin accelerates wound healing through a gradual mechanism, starting with the enhancement of angiogenesis and collagen production in the early phase (day 5) and followed by accelerated epithelialization in the later phase (day 10). Its roles as an antioxidant, anti-inflammatory, and regenerative agent underscore its potential for developing safe and effective herbal-based topical therapies.

However, the study has limitations that must be considered. The relatively small sample size may affect statistical power and generalizability. Although key histological parameters were analyzed, specific molecular expressions such as VEGF or TGF-β, as well as enzymatic activities relevant to wound healing, were not evaluated. Furthermore, the study's focus was limited to day 10, omitting longer-term maturation and remodeling phases. Future studies should employ longitudinal designs and biomolecular approaches to further substantiate these findings.

CONCLUSION

In conclusion, the findings of this study clearly demonstrate the beneficial effects of topical α-mangostin (Garcinia mangostana Linn.) on wound healing in a full-thickness rat model. The treatment significantly enhanced epithelial thickness, angiogenesis, and collagen density, particularly noticeable by day 10. These results suggest that α-mangostin not only promotes the initial stages of healing, such as angiogenesis by day 5, but also facilitates later stages like epithelialization and collagen formation, contributing to the overall strength and integrity of the healed tissue. By highlighting the compound's multifaceted role in promoting wound healing, this study opens avenues for further research into its potential as a safe and effective herbal therapy. Future studies should aim to elucidate the specific molecular mechanisms involved and consider longer-term outcomes, further solidifying α-mangostin's role in wound care applications.

DECLARATIONS

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Competing and conflicting interests

The authors declare no competing interests or conflicts of interest related to this work.

Ethical approval

Ethical approval for this study was granted by the Airlangga University Animal Care and Use Committee (No. 2.KEH.61.04.2025), confirming adherence to ethical standards in the treatment of animal subjects.

Informed consent

Not applicable.

REFERENCES

1. Herman TF, Popowicz P, Bordoni B. Wound classification. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
2. Okur ME, Karantas ID, Şenyiğit Z, Üstündağ Okur N, Siafaka PI. Recent trends on wound management: New therapeutic choices based on polymeric carriers. Asian Journal of Pharmaceutical Sciences. 2020;15(6):661–684.
3. Nour S, Baheiraei N, Imani R, Khodaei M, Alizadeh A, Rabiee N, Moazzeni SM. A review of accelerated wound healing approaches: biomaterial-assisted tissue remodeling. Journal of Materials Science: Materials in Medicine. 2019;30(10):120.
4. Visha MG, Karunagaran M. A review on wound healing. International Journal of Clinicopathological Correlation. 2019;3:50–59.
5. Canonico S, Campitiello F, Della A, Padovano V, Pellino G. Treatment of leg chronic wounds with dermal substitutes and thin skin grafts. InTech; 2013.
6. Metcalfe AD, Ferguson MW. Tissue engineering of replacement skin: the crossroads of biomaterials, wound healing, embryonic development, stem cells and regeneration. Journal of the Royal Society Interface. 2007;4(14):413–437.
7. Dira D, Yanuarista Y, Afrianti R. Uji aktivitas ekstrak pericarp kulit buah manggis terpurifikasi dalam penyembuhan luka eksisi. TALENTA Conference Series: Tropical Medicine. 2018;1:134–138.
8. Tran VA, Vo TT, Nguyen MT, Dat ND, Doan V, Nguyen T, Vu QH, Le VT, Tong TD. Novel α-mangostin derivatives from mangosteen (Garcinia mangostana L.) peel extract with antioxidant and anticancer potential. Journal of Chemistry. 2021;1.
9. Wathoni N, Sari DP, Suharyani I, Motoyama K, Mohammed AFA, Cahyanto A, Abdassah M, Muchtaridi M. Enhancement of α-mangostin wound healing ability by complexation with 2-hydroxypropyl-β-cyclodextrin in hydrogel formulation. Pharmaceuticals. 2020;13:1–16.
10. Tantra I, Rizqiawan A, Putu N, Sumarta M. Alpha-Mangostin as potent osteogenesis and anti-inflammation bioactive material – Literature review. Natural Volatiles and Essential Oils. 2021;8:4875–4884.
11. Khairani TN, Rumanti RM, Manao A. Formulasi sediaan krim ekstrak etanol kulit buah manggis (Garcinia mangostana L.) sebagai obat luka bakar pada tikus putih jantan. Jurnal Ilmiah Farmasi Alauddin. 2020;4:53-58.

12. Charan J, Kantharia ND. How to calculate sample size in animal studies. Journal of Pharmacology and Pharmacotherapy. 2013;4(4):303-306.
13. Gunawan SA, Berata I, Wirata I. Histopatologi kulit pada kesembuhan luka insisi tikus putih pasca pemberian extracellular matrix (ECM) yang berasal dari vesica urinaria babi. Indonesian Medicus Veterinus. 2019;8(3):313-324.
14. Arisanty IP. Konsep dasar manajemen perawatan luka. Jakarta: Buku Kedokteran EGC; 2011.
15. Johnson KE, Wilgus TA. Vascular endothelial growth factor and angiogenesis in the regulation of cutaneous wound repair. Advances in Wound Care (New Rochelle). 2014;3(10):647–661.
16. Pedraza-Chaverri J, Cárdenas-Rodríguez N, Orozco-Ibarra M, Pérez-Rojas JM. Medicinal properties of mangosteen (Garcinia mangostana). Food and Chemical Toxicology: An International Journal Published for the British Industrial Biological Research Association. 2008;46(10):3227-3239.
17. Jittiporn K, Suwanpradid J, Patel C, Rojas M, Thirawarapan S, Moongkarndi P, Suvitayavat W, Caldwell RB. Anti-angiogenic actions of the mangosteen polyphenolic xanthone derivative α-mangostin. Microvascular Research. 2014;93:72–79.
18. Diller RB, Tabor AJ. The role of the extracellular matrix (ECM) in wound healing: A review. Biomimetics (Basel, Switzerland). 2022;7(3):87.
19. Ilhami R, Sanubari RT, Dira D. Pemeriksaan kadar hidroksiprolin dan uji aktivitas alfa-mangostin terhadap penyembuhan luka pada tikus putih jantan. Thesis. STIFI Perintis Padang; 2017.
20. Huang K, Mi B, Xiong Y, Fu Z, Zhou W, Liu W, Liu G, Dai G. Angiogenesis during diabetic wound repair: from mechanism to therapy opportunity. Burns & Trauma. 2025;13.