Original Article

Efficacy of Kelulut Bee Propolis Extract–Based Dressings on Wound Healing in Diabetic Rats: A Preclinical Study

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Abstract

Introduction: **Diabetic ulcers require effective management to prevent complications. Kelulut bee propolis, rich in flavonoids and phenolic acids, offers significant potential for wound care. This study evaluated the efficacy of standardised Kelulut bee propolis extract–based dressings on wound healing in diabetic rats.**

Methods: **Twenty-four male Wistar rats (*n* = 6 per group) were divided into healthy control (Group I), diabetic control (Group II), povidone-iodine (Group III), and 20% (w/v) propolis dressing (50 mg/pad) (Group IV). Diabetes was induced using alloxan (150 mg/kg body weight). Wounds were measured daily for 20 days using digital callipers under a single-blind procedure to minimise bias. Data were analysed using repeated measures analysis of variance (RM-ANOVA) and post-hoc least significant difference (LSD) tests ($P < 0.05$).**

Results: **Group IV showed the most rapid contraction. By Day 5, Group IV's mean incision length (0.55 ± 0.22 cm) was significantly lower than Group II (1.70 ± 0.17 cm; $P = 0.001$). Group IV achieved complete closure by Day 10, significantly faster than Group II (1.28 ± 0.24 cm) and Group III (0.27 ± 0.11 cm). RM-ANOVA confirmed significant differences between groups [$F(3, 20) = 48.72$; $P = 0.001$]. LSD tests validated propolis's superiority over povidone-iodine ($P = 0.003$).**

Conclusion: **Standardised 20% Kelulut propolis dressings significantly accelerate diabetic wound healing in rats compared to povidone-iodine. These preclinical findings suggest that propolis effectively modulates the hyperglycemic microenvironment. However, further human clinical trials are essential to validate safety and dosage before clinical implementation.**

Keywords: *Kelulut bee propolis, diabetic wound healing, propolis-based dressing, diabetic rat model, wound dressing*

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Introduction

Diabetes mellitus (DM) is a complex metabolic disorder characterised by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The global epidemiological burden is substantial, with Indonesia projected to reach 23.1 million cases by 2030 (1). Often termed a "silent killer," DM can lead to severe systemic complications, including visual impairment, cardiovascular disease, and notably, chronic non-healing wounds known as diabetic ulcers. These ulcers are highly susceptible to bacterial infection and, if left untreated, may progress to diabetic gangrene and ultimately require amputation (2).

Current clinical management often relies on conventional antiseptic dressings, such as povidone-iodine (3). Although effective at preventing infection, povidone-iodine has been reported to exhibit cytotoxicity toward fibroblasts, which may paradoxically delay re-epithelialisation in fragile diabetic tissues (4). Consequently, there is an urgent need to identify bioactive natural alternatives that not only provide antimicrobial protection but also actively promote tissue regeneration (5).

Kelulut propolis, sourced from stingless bees in the biodiversity-rich region of East Kalimantan, Indonesia, has emerged as a promising therapeutic candidate (6). Although propolis is frequently discarded as a byproduct of honey production, phytochemical screening reveals that it is exceptionally rich in bioactive constituents, including triterpenoid saponins, steroids, and, in particular, high concentrations of flavonoids and phenolic acids (7).

A critical research gap exists regarding the application of stingless bee propolis in diabetic wound care (8). While the therapeutic effects of *Apis mellifera* propolis are well documented, Kelulut propolis possesses a unique geobotanical chemical profile that may offer superior efficacy in modulating the impaired wound microenvironment in hyperglycemic subjects (9). Scientifically, the delayed healing in diabetes is driven by a persistent inflammatory state and excessive oxidative stress (10). The flavonoids and phenolic acids found in Kelulut propolis are hypothesised to act as potent modulators that can inhibit pro-inflammatory cytokines, such as TNF-α and IL-6, thereby facilitating the essential transition from the inflammatory phase to the proliferative and remodelling stages (11).

Despite these theoretical benefits, empirical evidence specifically validating the efficacy of Kelulut bee propolis extract–based dressings in standardised diabetic models remains limited (12). Therefore, this study aims to establish a rigorous preclinical foundation by evaluating the effectiveness of these dressings in accelerating wound contraction and re-epithelialisation in alloxan-induced diabetic rats. These findings are intended to provide the necessary scientific evidence for the future development of advanced, natural bioactive interventions in chronic wound management.

Methods

Materials

The primary biological material for the intervention was raw Kelulut bee propolis, sourced from local meliponiculture apiaries in Samarinda, East Kalimantan (13). The study utilised 24 male Wistar rats (*Rattus norvegicus*), aged 2–3 months with a body weight of 250–300 grams (14). Alloxan Monohydrate was employed for intraperitoneal induction to establish the diabetic model (15). Surgical procedures and data collection utilised sterile scalpels for standardised incisions, a digital glucometer for blood glucose monitoring, and a calibrated digital vernier calliper with 0.01 mm precision for wound closure measurement (16).

Research Design

This study employed a true experimental laboratory design with a post-test-only control group approach (17). This design was chosen to determine the causality and effectiveness of the intervention by comparing the outcome (wound healing) between the experimental group receiving the propolis dressing and the control group under controlled laboratory conditions.

Setting and Samples

The study was conducted at the Biomedical Science Laboratory of a private university in East Kalimantan, Indonesia, from 1 September to 30 September 2025. A total of 24 male

Wistar rats were selected and allocated into four groups (n = 6 per group) using a simple random sampling technique (18). The sample size was determined using the Federer formula to ensure sufficient statistical validity for preclinical trials. Specific inclusion and exclusion criteria were applied to ensure subject health and consistency across the experimental units (19).

Intervention

Subjects were acclimatised and fasted for 16 to 18 h before the induction of diabetes via a single intraperitoneal injection of alloxan monohydrate (150 mg/kg body weight). Diabetic status was confirmed three days post-injection for rats with glucose levels > 200 mg/dL (20). Before the surgical procedure, the dorsal area of each rat was pre-shaved and anaesthetised with topical lidocaine cream to ensure adequate pain management and minimise distress during wound creation. After anaesthesia onset, standardised dorsal incisions (2 cm in length and approximately 3 mm in depth) were created with a sterile scalpel; bleeding confirmed a full-thickness wound. This procedure was conducted in strict accordance with the Refinement principle of the 3Rs, prioritising animal welfare throughout the experimental phase (21). Subjects were divided into: Group I (healthy control), Group II (diabetic control), Group III (positive control – povidone-iodine), and Group IV (experimental – Kelulut bee propolis extract–based dressings). The interventions were carried out daily for 20 days and involved cleaning the wound area and applying the respective treatment materials strictly according to the group assignment. Specifically, the wounds in Group I (healthy control) and Group II (diabetic control) were cleaned and dressed daily with sterile normal saline (0.9% NaCl) (22).

Preparation of Kelulut Propolis Extract and Dressings

The extraction utilised maceration with 70% ethanol at a 1:10 (w/v) ratio for three days in the dark. The filtrate was concentrated using a rotary evaporator and subsequently partitioned with ethyl acetate to isolate the bioactive viscous extract (23). To ensure reproducibility, the extract was standardised to 20% (w/v), consistent with previous topical applications of propolis extracts that demonstrated successful wound healing in diabetic rat models (15, 24). Therapeutic dressings were prepared by submerging sterile 1 cm × 1 cm pads in this standardised extract for 24 h to facilitate complete fibre saturation (25). Gravimetric analysis confirmed that each pad held approximately 50 mg of the propolis fraction. Dressings were stored aseptically in aluminium foil until application (26).

Measurement and Data Collection

The primary outcome was the reduction in wound length, measured daily for 20 days using a digital vernier calliper (27). Although the wounds were monitored daily, data extraction and formal assessment of healing progression were performed on Day 1 (baseline), Day 5 (inflammatory phase), Day 10 (proliferative phase), and Day 15 (remodelling phase) to map the healing kinetics. To minimise measurement bias, a single-blind procedure was implemented, with the primary researcher responsible for wound assessment blinded to group assignments. Consistency was further maintained by having the same observer assess the wounds at the same time each day (28).

Data Analysis

Data were summarised using mean and standard deviation (mean ± SD). Normality and homogeneity were assessed using the Shapiro–Wilk and Levene's tests, respectively (29). Due to the longitudinal nature of the data, the interaction between treatment groups and time was evaluated using repeated measures analysis of variance (RM-ANOVA) to ensure a more accurate representation of healing kinetics than a standard one-way ANOVA. Post-hoc pairwise comparisons were conducted using the least significant difference (LSD) test, with $P < 0.05$ considered statistically significant (30).

Results

Wound Closure Kinetics and Macroscopic Observations

The macroscopic evaluation of the dorsal incisions revealed a progressive reduction in mean wound length across all four experimental groups over the 20-day observation period. At baseline (Day 1), incision lengths did not differ significantly between groups, with mean values ranging from 1.84 ± 0.23 cm to 1.88 ± 0.41 cm, confirming a standardised initial wound model. As the study progressed into the inflammatory phase (Day 5), the Kelulut bee propolis extract–

based dressing group (Group IV) exhibited accelerated wound contraction (0.55 ± 0.22 cm) compared to the diabetic control group (1.70 ± 0.17 cm) and the povidone-iodine group (0.94 ± 0.28 cm). By the proliferation phase (Day 10), Group IV achieved complete wound closure (0.00 ± 0.00 cm), whereas the diabetic control (Group II) maintained a significantly larger unhealed area (1.28 ± 0.24 cm). The povidone-iodine group (Group III) achieved complete closure by Day 15, while the untreated diabetic group failed to achieve full epithelialisation even by Day 20 (31). Figure 1 visually summarises the longitudinal progression of healing. Figure 2 illustrates the representative macroscopic changes in wound contraction observed across the experimental groups.

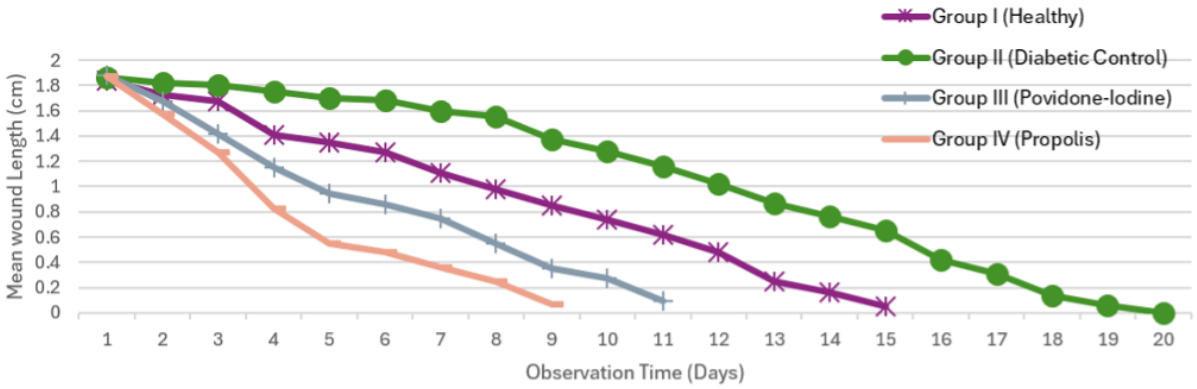


Figure 1. Wound-healing kinetics and longitudinal progression in diabetic rat models.

Data are expressed as mean ± SD (n = 6 per group). Group IV (propolis) demonstrated significantly faster wound closure than diabetic control (Group II) and povidone-iodine (Group III). Statistical markers indicate significance at $P < 0.05$ using RM-ANOVA followed by LSD post-hoc tests.

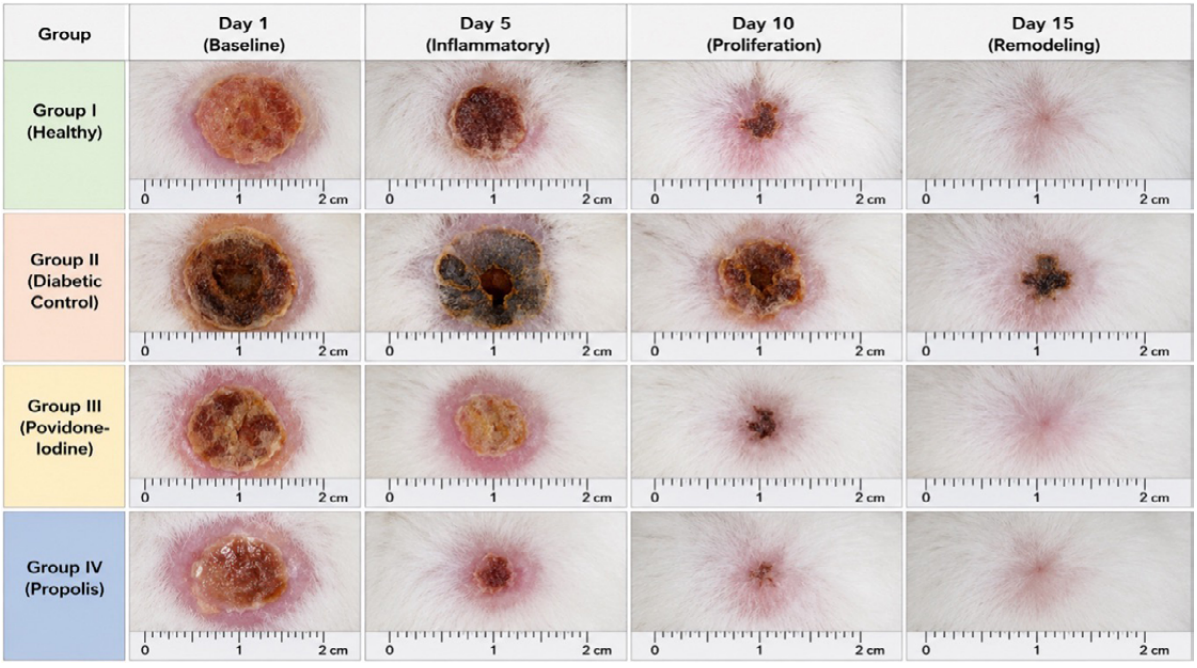


Figure 2. Representative macroscopic photographs of wound-healing progression in Wistar rats on days 1, 5, 10, and 15 across experimental groups: Group I (healthy control), Group II (diabetic control), Group III (povidone-iodine), and Group IV (Kelulut bee propolis extract–based dressings).

Wound-healing phases were categorised as baseline (Day 1), inflammatory (Day 5), proliferative (Day 10), and remodelling (Day 15) based on observed macroscopic progression.

Statistical Validation of Healing Efficacy

To address the longitudinal nature of the measurements, a repeated measures analysis of variance (RM-ANOVA) was performed, revealing a significant main effect for the treatment group [F (3, 20) = 48.72; P = 0.001] and a significant group × time interaction, indicating that the rate of healing was dependent on the type of dressing applied over the 20-day period (32). The mean incision lengths at critical time intervals, along with statistical values, are summarised in Table 1.

Post-hoc pairwise comparisons using the LSD test confirmed that the healing rate in the Kelulut bee propolis extract–based dressing group was significantly faster than in the diabetic control (P = 0.001) (33). Furthermore, the propolis-based intervention demonstrated a statistically significant advantage over the standard povidone-iodine treatment (P = 0.003). Significant differences were also recorded between the healthy control (Group I) and the diabetic control (Group II) (P = 0.004), validating the experimental model's sensitivity to hyperglycemic wound stagnation (34). Table 2 presents the detailed matrix of these pairwise statistical comparisons.

Discussion

The primary objective of this study was to evaluate the efficacy of Kelulut bee propolis extract–based dressings on wound-healing kinetics in diabetic rats, providing a preclinical foundation for innovative wound care interventions (35). Our findings show that standardised propolis dressings significantly accelerated wound closure compared with both diabetic controls and standard povidone-iodine treatment (36). Based on longitudinal observation, Group IV (propolis) achieved complete wound epithelialisation by an average of Day 10, which was statistically superior to povidone-iodine (P = 0.003) and the diabetic control group, which failed to achieve closure within the 20-day period (37).

Scientifically, the accelerated healing observed in the propolis group can be attributed to its rich flavonoid and phenolic acid composition, which possesses potent anti-inflammatory and antioxidant properties (38). While specific molecular pathways—such as the inhibition of pro-inflammatory cytokines (TNF-α and IL-6) or the stimulation of growth factors

Table 1. Longitudinal evaluation of mean wound incision length (cm) in alloxan-induced diabetic rats across treatment groups (Days 1 to 15).

Group	Day 1 (baseline)	Day 5 (inflammatory)	Day 10 (proliferation)	Day 15 (remodelling)	Normality (P)	ANOVA (P)
Group I (healthy)	1.84 ± 0.23	1.35 ± 0.24	0.74 ± 0.27	0.05 ± 0.02	0.063	0.001*
Group II (diabetic)	1.86 ± 0.07	1.70 ± 0.17	1.28 ± 0.24	0.65 ± 0.25	0.165	
Group III (povidone)	1.88 ± 0.41	0.94 ± 0.28	0.27 ± 0.11	0.00 ± 0.00	0.415	
Group IV (propolis)	1.87 ± 0.57	0.55 ± 0.22	0.00 ± 0.00	0.00 ± 0.00	0.431	

Data are presented as mean ± standard deviation (n = 6 per group). F (3, 20) = 48.72, P = 0.001 using repeated measures ANOVA.

Table 2. Post-hoc pairwise comparison matrix (least significant difference test) for wound-healing efficacy between healthy, diabetic, povidone-iodine, and propolis-treated groups.

Group	Group I (healthy)	Group II (diabetic)	Group III (povidone)	Group IV (propolis)
Group I (healthy)	—	0.004*	0.001*	0.001*
Group II (diabetic)	0.004*	—	0.002*	0.001*
Group III (povidone)	0.001*	0.002*	—	0.003*
Group IV (propolis)	0.001*	0.001*	0.003*	—

P-values are obtained from the least significant difference post-hoc test following repeated measures ANOVA; * indicates statistical significance at the $P < 0.05$ level. Data represent comparisons between six animals per group (n = 6).

(VEGF and TGF-β)—were not experimentally quantified in this study, they are hypothesised to be the primary drivers of the observed regeneration, based on established literature on Kelulut propolis (39). The data suggest that the propolis intervention effectively mitigated hyperglycemia-induced oxidative stress, facilitating a swift transition from the chronic inflammatory phase to the proliferative phase of healing (40).

A critical finding of this study is the statistical superiority of propolis over povidone-iodine (41). While povidone-iodine remains a conventional antiseptic standard, its potential cytotoxicity toward fibroblasts may inadvertently retard the rate of tissue regeneration (42). In contrast, the Kelulut bee propolis extract–based dressing supported rapid re-epithelialisation without such retardation, indicating its role as a "pro-healing" agent rather than a mere antiseptic (43). The validity of the experimental model was further confirmed by the significant difference between healthy and diabetic controls (P = 0.004), which accurately reflects the wound stagnation typically seen in hyperglycemic states (44).

Several limitations of this study must be acknowledged. First, the sample size was relatively small (n = 6 per group), which, while statistically valid under the Federer formula, may limit the generalisability of the findings (45). Second, the assessment was limited to macroscopic wound-length measurements. The absence of histopathological analysis (to evaluate collagen deposition) and molecular markers (to measure specific cytokine levels) means that the underlying biological mechanisms remain inferential (46). Future research utilising larger cohorts and histological endpoints is necessary to provide a more granular understanding of propolis-mediated tissue repair (47).

From a clinical practice perspective, these findings offer promising evidence for the development of bioactive, natural dressings that minimise chemical irritation in chronic wound management (48). However, it is important to note that these results are derived from a preclinical animal model (49). Before these findings can be integrated into clinical protocols, further human clinical trials are required to determine optimal dosage, safety profiles, and patient comfort (50). This study serves as an essential stepping stone toward standardising Kelulut propolis as a cost-effective, indigenous resource for advanced diabetic wound care (51).

Conclusion

This study demonstrates that standardised Kelulut bee propolis extract–based dressings (20% w/v) significantly accelerate wound healing in diabetic rats, achieving superior contraction and complete closure markedly faster than conventional povidone-iodine treatments. The extract's bioactive capacity to modulate the diabetic wound microenvironment and resolve chronic inflammatory delays is likely responsible for this therapeutic efficacy. However, as these findings are derived from a preclinical animal model with a small sample size (n = 6 per group), they should be interpreted as preliminary evidence rather than definitive clinical proof. While Kelulut propolis shows promising potential as a bioactive alternative in advanced wound care, further human clinical trials are essential to validate its safety, optimal dosage, and clinical efficacy before it can be cautiously integrated into standard nursing practice protocols.

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Ethics of Study

The study followed the 3Rs principles of animal welfare and received approval from the Health Research Ethics Committee of the Health Polytechnic, East Kalimantan (Ref: DP.04.03/F.XXXVI.25/284/2025).

Conflict of Interest

None.

Funds

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Authors' Contributions

Conception and design: ABS
Analysis and interpretation of the data: ABS
Drafting of the article: ABS
Critical revision of the article for important intellectual content: ABS
Final approval of the article: TS
Provision of study materials or patients: TS
Statistical expertise: PMK
Obtaining of funding: PMK
Administrative, technical, or logistic support: USMR
Collection and assembly of data: USMR

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References

1. Cloete L. Diabetes mellitus: an overview of the types, symptoms, complications and management. *Nurs Stand*. 2022;**37(1)**:61–66. https://doi.org/10.7748/ns.2021.e11709

2. Salrian AA, Behzadi A, Oloumi MM, Farajli Abbasi M, Delshad S, Moghadaszadeh M. Amplification of wound healing by propolis and honey ointment in healthy and diabetic rat models: histopathological and morphometric findings. *Arch Razi Inst*. 2022;**77(5)**:1673–1681. https://doi.org/10.22092/ARI.2022.357191.1991

3. Takzaree N, Hadjiakhondi A, Hassanzadeh G, Rouini MR, Manayi A. Synergistic effects of honey and propolis on cutaneous wound healing in rats. *Acta Med Iran*. 2016;**54(4)**:233–239.

4. Jusril NA, Mohd KS, Mutalib NA, Badiazaman AAM. Chemical composition and pharmacological aspects of Malaysian stingless bee propolis: an up-to-date systematic review. *Biomed Rep*. 2024;**22(1)**:9. https://doi.org/10.3892/br.2024.1887

5. Osonoi S, Hamaura K, Murakami H. A diabetic patient with finger gangrene. *Eur J Intern Med*. 2022;**103**:100–101. https://doi.org/10.1016/j.ejim.2022.05.006

6. Jiang P, Li Q, Luo Y, Luo F, Che Q, Lu Z, et al. Current status and progress in research on dressing management for diabetic foot ulcer. *Front Endocrinol*. 2023;**14**:1221705. https://doi.org/10.3389/fendo.2023.1221705

7. Sahlan M, Mahira KF, Wiratama I, Mahadewi AG, Yohda M, Hermansyah H, et al. Purification and characterization of proteins in multifloral honey from Kelulut bee (stingless bee). *Heliyon*. 2019;**5(11)**:e02835. https://doi.org/10.1016/j.heliyon.2019.e02835

8. Kustiawan PM, Siregar KAAK, Syaifie PH, Zein Muttaqin F, Ibadillah D, Miftah Jauhar M, et al. Uncovering the anti-breast cancer activity potential of East Kalimantan propolis by in vitro and bioinformatics analysis. *Heliyon*. 2024;**10(13)**:e33636. https://doi.org/10.1016/j.heliyon.2024.e33636

9. Fahrurroji A, Suhandi C, Chaerunisaa AY, Pratiwi L, Sriwidodo S. Natural bioactive-based advanced wound dressings for diabetic wound healing: a systematic review of emerging biomaterial platforms. *Int J Nanomedicine*. 2026;**21**:588990. https://doi.org/10.2147/IJN.S588990

10. El-Sakhawy M, Salama A, Tohamy HS. Applications of propolis-based materials in wound healing. *Arch Dermatol Res*. 2023;**316(1)**:61. https://doi.org/10.1007/s00403-023-02789-x

11. Oryan A, Alemzadeh E, Moshiri A. Potential role of propolis in wound healing: biological properties and therapeutic activities. *Biomed Pharmacother*. 2018;**98**:469–483. https://doi.org/10.1016/j.biopha.2017.12.069

12. Zulhendri F, Chandrasekaran K, Kowalcz M, Ravalia M, Kripal K, Fearnley J, et al. Antiviral, antibacterial, antifungal, and antiparasitic properties of propolis: a review. *Foods*. 2021;**10(6)**:1360. https://doi.org/10.3390/foods10061360

13. Stevanović J, Glavinić U, Ristanić M, Erjavec V, Denk B, Dolašević S, et al. Bee-inspired healing: apitherapy in veterinary medicine for maintenance and improvement animal health and well-being. *Pharmaceuticals*. 2024;**17(8)**:1050. https://doi.org/10.3390/ph17081050

14. Pahlavani N, Malekahmadi M, Firouzi S, Rostami D, Sedaghat A, Bagheri Moghaddam A, et al. Molecular and cellular mechanisms of the effects of propolis in inflammation, oxidative stress and glycemic control in chronic diseases. *Nutr Metab*. 2020;**17**:65. https://doi.org/10.1186/s12986-020-00485-5

15. Hozzein WN, Badr G, Al Ghamdi AA, Sayed A, Al-Waili NS, Garraud O. Topical application of propolis enhances cutaneous wound healing by promoting TGF-beta/Smad-mediated collagen production in a streptozotocin-induced type I diabetic mouse model. *Cell Physiol Biochem*. 2015;**37(3)**:940–954. https://doi.org/10.1159/000430221

16. Manginstar CO, Tallei TE, Niode NJ, Salaki CL, Hessel SS. Therapeutic potential of propolis in alleviating inflammatory response and promoting wound healing in skin burn. *Phytother Res*. 2024;**38(2)**:856–879. https://doi.org/10.1002/ptr.8092

17. Slater P, Hasson F. Quantitative research designs, hierarchy of evidence and validity. *J Psychiatr Ment Health Nurs*. 2025;**32(3)**:656–660. https://doi.org/10.1111/jpm.13135

18. Titova AA, Mavlikeev MO, Kaligin MS, Suleymanova DM, Chekmaryeva IA, Kiyasov AP, et al. Early ultra- and microstructural alterations in rat pancreas in alloxan-induced diabetes mellitus. *Ultrastruct Pathol*. 2020;**44(1)**:61–70. https://doi.org/10.1080/01913123.2019.1710313

19. Lee KM, Wason J. Design of experiments for a confirmatory trial of precision medicine. *J Stat Plann Inference*. 2019;**199**:179–187. https://doi.org/10.1016/j.jspi.2018.06.004

20. Garcia-Perez E, Schönberger T, Sumalla M, Stierstorfer B, Solà R, Doods H, et al. Behavioural, morphological and electrophysiological assessment of the effects of type 2 diabetes mellitus on large and small nerve fibres in Zucker diabetic fatty, Zucker lean and Wistar rats. *Eur J Pain*. 2018;**22(8)**:1457–1472. https://doi.org/10.1002/ejp.1235

21. Qin X, Ding B, Li Y. Herbal multicomponent extracts enhance wound healing after incision of perianal abscess and in a rat model of infected wounds. *Australas J Dermatol*. 2018;**59(1)**:76–78. https://doi.org/10.1111/ajd.12663

22. Farsak M, Özdağli G, Özmüş D, Çömelekoğlu Ü, Yalın S, Bozdoğan Arpacı R, et al. Effects of *Hypericum perforatum* on an experimentally induced diabetic wound in a rat model. *Wounds*. 2017;**29(2)**:E10–E17.

23. Abu-Seida AM. Effect of propolis on experimental cutaneous wound healing in dogs. *Vet Med Int*. 2015;**2015(1)**:672643. https://doi.org/10.1155/2015/672643

24. Faria TF, Faria RF, Kamada I, BL. Topical use of green propolis for wound healing: a systematic review of the literature. *ESTIMA Braz J Enterostomal Ther*. 2022;**20**:e0222. https://doi.org/10.30886/estima.v20.1135_IN

25. Musdalifah, Djide MN, Ida N. The effect of propolis extract concentration in ointment preparations on the growth inhibition of *Staphylococcus aureus* bacteria. *Maj Farm Farmakol*. 2021;**25(2)**:73–75.

26. Zeng Q, Qi X, Shi G, Zhang M, Haick H. Wound dressing: from nanomaterials to diagnostic dressings and healing evaluations. *ACS Nano*. 2022;**16(2)**:1708–1733. https://doi.org/10.1021/acsnano.1c08411

27. Khoo R, Jansen S. The evolving field of wound measurement techniques: a literature review. *Wounds*. 2016;**28(6)**:175–181.

28. Turi GK, Donovan V, DiGregorio J, Criscitelli TM, Kashan B, Barrientos S, et al. Major histopathologic diagnoses of chronic wounds. *Adv Skin Wound Care*. 2016;**29(8)**:376–382. https://doi.org/10.1097/01.ASW.0000484665.45022.b3

29. Poddiakov A. Creativity of creativity researchers: invention of problems and experimental objects to study thinking. *Integr Psychol Behav Sci*. 2023;**57(1)**:43–64. https://doi.org/10.1007/s12124-022-09713-4

30. Schutte T, Fasel ME, Fokkens JT, Wouters A. The reporting of ethical review and ethical considerations in articles published in medical education journals: a literature review. *Med Educ*. 2023;**57(9)**:870–878. https://doi.org/10.1111/medu.15139

31. Alven S, Aderibigbe BA. Chitosan and cellulose-based hydrogels for wound management. *Int J Mol Sci*. 2020;**21(24)**:9656. https://doi.org/10.3390/ijms21249656

32. Fajari NM, Pranoto A, Perdanakusuma DS, Prenggono MD, Rudiansyah M, Nur'amin HW, et al. Comparison of stingless bee honey and silver sulfadiazine on diabetic wound healing in rat models. *Med J Indones*. 2025;**34(3)**:151–157. https://doi.org/10.13181/mji.oa.257974

33. Franca JR, De Luca MP, Ribeiro TG, Castilho RO, Moreira AN, Santos VR, et al. Propolis-based chitosan varnish: drug delivery, controlled release and antimicrobial activity against oral pathogen bacteria. *BMC Complement Altern Med*. 2014;**14**:478. https://doi.org/10.1186/1472-6882-14-478

34. Sanlier N, Kaya EY, Yucel II. Health effects of bee products: a comprehensive review. *Food Sci Nutr*. 2026;**14(2)**:e71165. https://doi.org/10.1002/fsn3.71165

35. Mele E. Electrospinning of honey and propolis for wound care. *Biotechnol Bioeng*. 2023;**120(5)**:1229–1240. https://doi.org/10.1002/bit.28341

36. Kustiawan PM, Syahbana MA, Pratika R, Ichsan MN, Mentari IA, Hairunnisa I, et al. Investigating the bioactivity potential and standardization of two stingless bee propolis from East Kalimantan. *Pharm Sci Res*. 2024;**11(3)**:143–155. https://doi.org/10.7454/psr.v11i3.1388

37. Buitrago DM, Perdomo SJ, Silva FA, Cely-Veloza W, Lafaurie GI. Physicochemical characterization, antioxidant, and proliferative activity of Colombian propolis extracts: a comparative study. *Molecules*. 2024;**29(7)**:1643. https://doi.org/10.3390/molecules29071643

38. Machado Velho JC, França TA, Malagutti-Ferreira MJ, Albuquerque ER, Lívero FADR, Soares MR, et al. Use of propolis for skin wound healing: systematic review and meta-analysis. *Arch Dermatol Res*. 2023;**315(4)**:943–955. https://doi.org/10.1007/s00403-022-02455-8

39. Setyawan AB, Satria AP, Arung ET, Paramita S. Effect of bee pollen kelulut bees on HbA1c in type 2 diabetes mellitus patients. *Malays J Fundam Appl Sci*. 2023;**19(1)**:56–60. https://doi.org/10.11113/mjfas.v19n1.2750

40. Chen RF, Wang CT, Chen YH, Chien CM, Lin SD, Lai CS, et al. Hyaluronic acid-povidone-iodine compound facilitates diabetic wound healing in a streptozotocin-induced diabetes rodent model. *Plast Reconstr Surg*. 2019;**143(5)**:1371–1382. https://doi.org/10.1097/PRS.0000000000005504

41. Lazo GL, Lemes DC, Pauletti PM, Bastos JK, Ambrósio SR, Veneziani RCS, et al. Analysis of the antimicrobial activity of propolis: a narrative review of in-vitro studies. *An Acad Bras Cienc*. 2025;**97(3)**:e20241302.

42. Sharifiaghdam M, Shaabani E, Faridi-Majidi R, De Smedt SC, Braeckmans K, Fraire JC. Macrophages as a therapeutic target to promote diabetic wound healing. *Mol Ther*. 2022;**30(9)**:2891–2908. https://doi.org/10.1016/j.ymthe.2022.07.016

43. Morais MS, Bonfim DPF, Aguiar ML, Oliveira WP. Electrospun poly (vinyl alcohol) nanofibrous mat loaded with green propolis extract, chitosan and nystatin as an innovative wound dressing material. *J Pharm Innov*. 2022;**(18)**;704–718. https://doi.org/10.1007/s12247-022-09681-7

44. Ferreira SRL, Teixeira SA, Lima GO, de Castro JNRS, Teixeira LEO, Barros CAR, et al. Healing activity of propolis of stingless bee (*Scaptotrigona* aff. *postica*), reared in monoculture of açaí (*Euterpe oleracea*), in induced wounds in rats. *Molecules*. 2024;**29(19)**:4742. https://doi.org/10.3390/molecules29194742

45. Alsarayrah NA, Mohamed R, Omar EA. Stingless bee propolis: a comprehensive review of chemical constituents and health efficacy. *Nat Prod Bioprospect*. 2025;**15(1)**:61. https://doi.org/10.1007/s13659-025-00545-4

46. Zayed HS, Saleh S, Omar AE, Saleh AK, Salama A, Tolba E. Development of collagen-chitosan dressing gel functionalized with propolis-zinc oxide nanoarchitectonics to accelerate wound healing. *Int J Biol Macromol*. 2024;**261(2)**:129665. https://doi.org/10.1016/j.ijbiomac.2024.129665

47. Ayoub WS, Ritu, Zahoor I, Dar AH, Farooq S, Mir TA, et al. Exploiting the polyphenolic potential of honey in the prevention of chronic diseases. *Food Chem Adv*. 2023;**3**:100373. https://doi.org/10.1016/j.focha.2023.100373

48. Setyawan AB, Mahadeva Rao US MSN. Therapeutic potential of stingless bee pollen: a review. *Syst Rev Pharm*. 2023;**16(5)**:2549–2556. https://doi.org/10.52711/0974-360X.2023.00419

49. Armstrong DG, Tan TW, Boulton AJM, Bus SA. Diabetic foot ulcers: a review. *JAMA*. 2023;**330(1)**:62–75. https://doi.org/10.1001/jama.2023.10578

50. Stojko M, Wolny D, Włodarczyk J. Nonwoven releasing propolis as a potential new wound healing method: a review. *Molecules*. 2021;**26(18)**:5701. https://doi.org/10.3390/molecules26185701

51. Subrata SA, Phuphaibul R. Diabetic foot ulcer care: a concept analysis of the term integrated into nursing practice. *Scand J Caring Sci*. 2019;**33(2)**:298–310. https://doi.org/10.1111/scs.12645