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REVIEW

A Review of Medicinal Plants from the Anak Dalam Tribe of Jambi: An Evaluation of Their Potential for Diabetic Wound Healing Effects—Current Status and Future Perspectives

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Abstract: The Anak Dalam tribe, popularly known as *Suku Anak Dalam* (SAD), is an indigenous community in the Jambi Province of Indonesia. The traditional knowledge within this group is deeply intertwined with forest resources, particularly regarding medicinal plants utilized for wound healing. Significantly, diabetic wounds are a severe complication of diabetes mellitus. These wounds are typically characterized by delayed healing processes, high susceptibility to infection, and an elevated risk of amputation. Accordingly, this review summarizes medicinal plants traditionally employed by the Anak Dalam community for various wound-related conditions. Beyond simple documentation, the study evaluates the potential relevance of these species as candidate sources for diabetic wound-healing research. In this study, a narrative literature review was conducted utilizing databases such as Scopus, ScienceDirect, PubMed, Google Scholar, and ResearchGate, covering publications released between 2015 and 2025. Altogether, 40 medicinal plants were examined. Specifically, several species (ie, *Anredera cordifolia, Centella asiatica, Psidium guajava*, and *Piper betle*) demonstrated pharmacological activities directly relevant to wound-healing processes. The primary phytochemical constituents identified across these studies are flavonoids, alkaloids, terpenoids, saponins, and phenolic compounds. Crucially, these compounds are reported to exhibit potent antioxidant, anti-inflammatory, and antibacterial activities. Furthermore, these substances support vital biological processes associated with tissue repair, such as fibroblast proliferation, collagen synthesis, angiogenesis, and re-epithelialization. Most existing evidence, however, is derived from in vitro assays, animal models, or indirect pharmacological investigations. Therefore, the findings of this review should be viewed as a basis for generating potential candidates rather than as definitive proof of established clinical efficacy. This review highlights the necessity of integrating ethnobotanical knowledge with rigorous pharmacological validation. Ultimately, such integration is essential to support future research into evidence-based herbal approaches for the management of diabetic wounds.

Keywords: diabetic wound healing, Anak Dalam tribe, medicinal plants, herbal medicine, traditional medicine

Introduction

Diabetes mellitus (DM) is a multifaceted global health crisis, defined by its high prevalence and significant contribution to the rising global burden of illness. This impact is clearly demonstrated by elevated disability-adjusted life years (DALYs) reported across various populations.[1] Currently, diabetes stands as one of the fastest-growing non-communicable diseases worldwide.[2] According to data from the International Diabetes Federation (IDF), an estimated 536.6 million adults worldwide suffered from the condition in 2021. This figure is projected to climb to 783.2 million by 2045, reaching a global prevalence of 12.2%.[3]

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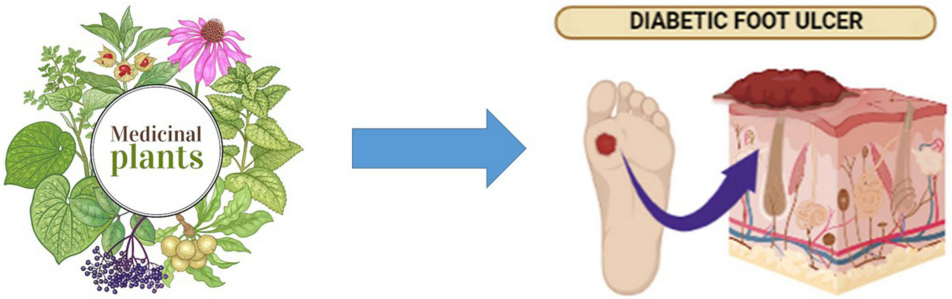
Graphical Abstract



Characteristically, the development of severe wounds, particularly diabetic foot ulcers, is a major complication in the long-term management of the disease. Epidemiological evidence suggests that 19% to 34% of patients with diabetes experience significant impairments in wound healing. Furthermore, approximately 20% of these individuals face an increased risk of lower-extremity amputation.[4,5] Impaired healing in diabetic patients stems primarily from the dysregulation of normal regenerative processes. This breakdown is driven by oxidative stress, peripheral neuropathy, and vascular dysfunction, which collectively result in delayed cellular proliferation and poor neo-tissue formation.[6,7] Such complications are worsened by the extended timeframe required for recovery, which commonly spans 12 to 13 months. With a healing success rate often falling below 80%, these issues substantially inflate medical expenses for patients and the healthcare system.[8]

Regardless of the wide implementation of standard therapeutic approaches for managing diabetic ulcers, conventional interventions often fall short. Standard treatments, including debridement, antibiotic therapy, and glycemic control, frequently prove insufficient to effectively accelerate tissue regeneration, particularly in patients suffering from severe vascular impairment.[9] Additionally, the necessity for prolonged antibiotic use may inadvertently heighten the risk of antibiotic resistance.[10] Therefore, there is an urgent need for complementary therapeutic approaches that promote effective, safe, and sustainable wound healing.

Natural products provide promising candidate sources for complementary wound management owing to their accessibility, chemical diversity, and extensive history of traditional use.[11] Principally, the therapeutic efficacy of medicinal plants is ascribed to their secondary metabolites, which exhibit potent antibacterial, antioxidant, and anti-inflammatory activities.[12] Research consistently demonstrates that bioactive compounds (eg, flavonoids, steroids, tannins, alkaloids, and terpenoids) play essential roles in critical biological processes. These include the regulation of inflammation, the promotion of angiogenesis and re-epithelialization, the management of oxidative stress, and the stimulation of cellular proliferation.[13,14]

The World Health Organization (WHO) estimates that approximately 80% of the global population relies on traditional medicine as a primary health resource.[15] Correspondingly, various nations have utilized plant-based remedies specifically for treating diabetic wounds, such as *Aster koraiensis* in Korea,[16] *Morinda citrifolia* L. in Vietnam,[17] and *Garcinia mangostana* L. in Thailand.[18] In Indonesia, vast biodiversity and rich local wisdom serve as foundational elements for developing nature-based alternative therapies. With over 300 ethnic groups, the nation possesses an extensive heritage of traditional medical knowledge, which frequently involves the application of medicinal plants to manage diabetes-related wounds.[19]

The Anak Dalam tribe, an indigenous community in Indonesia, maintains a prominent ethnomedical system with its largest population concentration located in Jambi Province.[20] Particularly, this community preserves a profound connection with forest ecosystems and ancestral territories, thereby cultivating a robust repository of traditional knowledge for treating various ailments, including wounds.[21] According to the studies analyzed in this review, 40 medicinal plant species have been documented as part of the Anak Dalam pharmacopeia for wound treatment. Notable examples include *Syzygium myrtifolium, Ocimum citriodorum, Centella asiatica, Zingiber cassumunar*, and *Curcuma zedoaria*.

The primary benefits of traditional medicinal plants used by the Anak Dalam tribe over conventional therapies include their multifunctional and synergistic properties, extensive empirical history, and distinctive biological activities.[22] Paradoxically, this traditional knowledge possesses cultural importance and the capacity to establish a scientific foundation for the development of effective, sustainable modern herbal medicines.

Even though medicinal plants used by the Anak Dalam tribe contain bioactive compounds relevant to wound-healing mechanisms, the available evidence remains largely preclinical, indirect, and heterogeneous. Correspondingly, this review summarizes medicinal plants traditionally used by the Anak Dalam tribe for wound-related conditions and evaluates their potential relevance as candidate sources for diabetic wound-healing research. By integrating ethnobotanical information with available pharmacological evidence, this review aims to identify promising plant candidates, highlight current evidence gaps, and propose future research directions.

Materials and Methods

Search Strategy

A comprehensive literature search was executed across several scientific databases, specifically Scopus, PubMed, ScienceDirect, SpringerLink, Google Scholar, ResearchGate, and other relevant Indonesian national databases such as Garuda and SINTA. To identify pertinent studies, the search strategy utilized a combination of keywords related to medicinal plant-based therapies for diabetic wound healing. These terms included "Anak Dalam Tribe" OR "medicinal plants" OR "herbal medicine" AND "diabetic wound healing."

Only articles available as full-text PDF files were considered for inclusion. Appropriately, duplicate records retrieved from multiple databases were removed before the initial screening process began. Particular emphasis was placed on studies reporting pharmacological activities and bioactive compounds that scientifically substantiate the traditional use of medicinal plants by the Anak Dalam tribe for managing diabetic wounds.

Data Selection and Collection Process

The literature selection process was carried out in several distinct stages to ensure the relevance and accuracy of the included studies. Initially, titles and abstracts were independently screened by the first author (APD) using Mendeley Desktop (Mendeley Ltd., London, UK) to organize references and eliminate duplicates. Subsequently, an eligibility assessment was conducted based on predefined inclusion criteria. These criteria required that (1) studies focus on medicinal plants from the Anak Dalam tribe in Jambi Province or plants with potential for healing diabetic ulcers, (2) the full text be accessible, (3) the articles be published between 2015 and 2025, and (4) the publications be written in English or Indonesian. Studies failing to meet these specific requirements were excluded. Conversely, studies deemed potentially relevant proceeded to the third stage, which involved a thorough full-text evaluation to confirm compliance with inclusion criteria and assess methodological quality. Any discrepancies or uncertainties arising during the screening were resolved through group discussions with MM, AYC, MAK, and AK until a consensus was achieved. Following the final selection of studies, data extraction and management were conducted systematically by APD. Finally, the selected articles were classified according to plant species, the parts used, types of biological assays, and reported mechanisms of action to facilitate a clear and structured analysis.

Data Synthesis

Data extracted from the eligible studies were systematically compiled and categorized based on the scientific names of the medicinal plants, reported pharmacological activities, identified bioactive compounds, and experimental models. Specifically, these models included in vitro, *in vivo*, or clinical assessments alongside observed outcomes related to diabetic wound healing. Due to the marked heterogeneity of study designs, plant species, and outcome measures, a quantitative meta-analysis proved unfeasible. Therefore, a qualitative narrative synthesis was conducted by systematically summarizing and comparing the findings across all included research. The data were grouped according to plant species, the parts utilized, types of biological assays, and reported mechanisms of action to identify consistent patterns. Additionally, the included studies were evaluated for methodological rigor, strength of evidence, and the relevance of

reported findings. Analytically, the synthesized data were examined to identify recurring interrelationships among plant species based on similarities in bioactive compounds, their reported mechanisms of action, and therapeutic effects, including antioxidant, anti-inflammatory, and antimicrobial activities.

Characteristics of Included Studies

The included studies primarily consisted of original research articles and review papers investigating the pharmacological properties of medicinal plants traditionally used by the Anak Dalam tribe. The therapeutic potential of each plant was assessed based on scientific evidence derived from antioxidant, anti-inflammatory, and antibacterial activity assays. Furthermore, this review highlights existing research gaps and emerging trends, particularly concerning plants that remain insufficiently explored from a pharmacological perspective. All included studies adhered to established principles of research ethics and academic integrity. Verifiable and peer-reviewed sources were utilized throughout the process to ensure the validity, transparency, and reproducibility of the findings.

Results and Discussion

Ethnobotanical Knowledge of the Anak Dalam Tribe

The Anak Dalam tribe (Indonesian: *Suku Anak Dalam* (SAD)) is an indigenous population residing in the forested regions of Jambi Province, Indonesia. Their livelihoods remain significantly reliant on forest resources for survival and cultural identity.[23] Geographically, the population is predominantly concentrated in Bukit Duabelas National Park, positioned between 102°30′00″ and 102°55′00″ East longitude and 1°45′00″ and 2°00′00″ South latitude. Additionally, a smaller segment of the community inhabits the southern region of Bukit Tiga Puluh National Park. Beyond these authorized conservation zones, the group is also found in secondary forests and oil palm plantation landscapes adjacent to the Trans-Sumatra Highway, stretching toward the border of South Sumatra Province.

Typically, the Anak Dalam tribe utilizes diverse forest plant resources to fulfill daily subsistence requirements, serve as trade commodities, and provide raw ingredients for traditional medicines.[24] According to the community's ethnomedical beliefs, medicinal plants used in traditional therapy are considered to possess minimal side effects while facilitating a progressive and holistic healing process.[25]

The Anak Dalam tribe possesses unique ethnobotanical knowledge regarding the medicinal application of plants, specifically for the treatment of wounds. Various traditional preparation and application methods are employed to maximize its efficacy. These include boiling leaves for topical washes, chewing plant material before applying it directly to the injury, and pounding leaves to extract sap or juice for application to the affected area.[26] Appropriately, commonly utilized plant parts are leaves, roots, rhizomes, fruit peels, fruits, stems, and sap.[27]

Table 1 presents medicinal plants traditionally used by the Anak Dalam tribe in Jambi Province and summarizes reported pharmacological activities that may be relevant to diabetic wound-healing research.

The reviewed literature indicates that the 40 medicinal plants associated with Anak Dalam traditional knowledge have been reported to exhibit pharmacological activities directly relevant to wound-healing processes. These include antioxidant, anti-inflammatory, and antibacterial activities. Paradoxically, these findings are derived from heterogeneous experimental models, and many plants have yet to be specifically evaluated in diabetic wound models. Therefore, the distribution of activities presented in Figure 1 should be interpreted as a descriptive summary of reported pharmacological evidence rather than a comparative measure of definitive efficacy.

Figure 1 summarizes the frequency of reported activities, with antioxidant activity being the most common at 33%, followed by antibacterial at 25%, and anti-inflammatory at 21%. Furthermore, wound healing-related activity accounts for 11%, while antidiabetic effects represent 10%. These percentages reflect the proportion of reported activities across the reviewed studies rather than quantitative measures of potency. Crucially, the data indicate that many plants exhibit multiple bioactivities. However, the type and extent of these reported effects vary significantly across plant species and experimental designs.

The Anak Dalam tribe has long relied on ethnopharmacological practices to manage various health conditions. In this review, these traditional wound-related uses are evaluated alongside pharmacological evidence through the utilization of

Table 1 Medicinal Plants Traditionally Used by the Anak Dalam Tribe and Their Reported Pharmacological Activities Related to Diabetic Wound Healing Research

No	Scientific Name/Family	Reported Activity	Sample Type	Extraction Solvent	Reported Compounds	Experimental Method	Main Findings	Reference
1.	*Syzygium myrtifolium*/ Myrtaceae	Antidiabetic	Fraction	Ethyl acetate, Water	Flavonoids, phenols, tannins, quinones, saponins, steroids/ triterpenoids	In vitro using pNPG (p-Nitrophenyl-β-D-glucopyranoside)	Ethyl acetate and aqueous fractions showed α-glucosidase inhibitory activity, with IC_{50} values of 0.40 ± 0.02 g/mL and 0.44 ± 0.03 g/mL, respectively	Nor et al[28]
		Antioxidant	Extract	Ethanol, Methanol, Water	Flavonoids, phenolics, saponins, terpenoids, alkaloids, tannins	DPPH (2,2-Diphenyl-1-picrylhydrazyl)	Ethanol extract of *Syzygium myrtifolium* leaves showed the highest activity compared to other parts, with 89.94% inhibition with IC_{50}= 11.87 µg/mL	Abdulrahman[29]
		Antibacterial	Extract	Chloroform, Ethyl acetate, Ethanol, Methanol and Water	Alkaloids, anthraquinones, flavonoids, phenolics, saponins, tannins, triterpenoids	Colorimetric broth microdilution with p-iodonitrotetrazolium chloride	Extracts showed bactericidal activity against selected bacterial strains, including *B. cereus, Staphylococcus aureus, A. baumannii*, and *K. pneumoniae.*	Ahmad et al[30]
2	*Ocimum citriodorum*/ Lamiaceae	Antioxidant and Anti-inflammatory	Extract	Distilled water (ultrasound-assisted extraction)	Alkaloids, saponins and steroids	DPPH (2,2-Diphenyl-1-picrylhydrazyl) and ABTS (2,2′-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid)	The IC_{50} of *Ocimum citriodorum* extract exhibited IC_{50} values of 20.80 ± 1.0 in the DPPH assay and 16.89 ± 0.5 in the ABTS assay. Its anti-inflammatory potential was further supported by pronounced lipoxygenase inhibitory activity and nitric oxide scavenging capacity.	Anusmitha et al[31]
3.	*Centella asiatica* / Apiaceae	Antioxidant	Extract	Methanol and Ethanol	Alkaloids, flavonoids, saponins and steroids	DPPH and ABTS	The methanolic extract of *C. asiatica* showed IC_{50} values of 40.7 ± 1.2 in the DPPH assay and 65.4 ± 1.2 in the ABTS assay, whereas the ethanolic extract exhibited IC_{50} values of 37.2 ± 1.2 against DPPH and 66.6 ± 0.3 against ABTS	Kandasamy et al[32]
4.	*Zingiber cassumunar*/ Zingiberaceae	Anti-inflammatory	Extract	Ethanol	Phenolic, terpenoid	Carrageenan 2%	*The Z. cassumunar* extract at concentrations of 2.5% and 5% showed no significant difference from 2.5% hydrocortisone cream in terms of anti-inflammatory efficacy, while the 1% extract also achieved inhibition levels exceeding 60%.	Wulansari et al[33]
5.	*Curcuma zedoaria*/ Zingiberaceae	Anti-inflammatory	Extract	Ethanol	Curcumin, sesquiterpenes, terpenoids, phenolic compounds	LPS (Lipopolysaccharide)	The crude extract of *Curcuma zedoaria* mitigated lipopolysaccharide (LPS)–induced neuronal cell loss by downregulating the expression of glial fibrillary acidic protein (GFAP) and interleukin-1β (IL-1β) in the hippocampal region.	Ayati et al[34]

(*Continued*)

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Table 1 (Continued).

No	Scientific Name/Family	Reported Activity	Sample Type	Extraction Solvent	Reported Compounds	Experimental Method	Main Findings	Reference
6.	*Kaempferia galanga*/ Zingiberaceae	Anti-inflammatory	Extract	Ethanol	Flavonoids, phenols, curcumin	In vivo male Wistar rats	Administration of *Kaempferia galanga* extract at a concentration of 0.5% effectively increased the percentage of ulcer area recovery and improved inflammatory marker scores. In addition, extract concentrations ranging from 0.5% to 2% were associated with a significant reduction in histopathological scores.	I. S. Wahyuni et al[35]
7.	*Dendrophthoe pentandra*/ Loranthaceae	Antioxidant	Extract	Ethanol	Alkaloids, phenols, tannins, saponins, steroids and terpenoids	DPPH	IC_{50} 49.10 µg/mL	Haryono et al[36]
8.	*Psidium guajava*/ Myrtaceae	Antibacterial	Extract	Water	Quercetin, tannin, routine, hesperidin	Disk diffusion, broth microdilution and MBC assays	MIC (Minimum inhibitory concentration): 6.8 mg/mL for all gram-positive bacteria MBC (Minimum bactericidal concentration): ≥ 11.4 mg/mL	Pereira et al[37]
9.	*Goniothalamus macrophyllus*/ Annonaceae	Antibacterial	Extract	Ethanol	Alkaloids, flavonoids, triterpenoids/steroids, saponins, tannins, phenols	Agar well diffusion	The root extract showed the strongest activity against *Candida albicans*, producing an inhibition zone of 12.9 mm at a concentration of 300 ppm, whereas the leaf extract was most effective against *Propionibacterium acnes*, with an inhibition zone of 22.7 mm at the same concentration. Both extracts also exhibited antibacterial activity against *Streptococcus mutans*, yielding inhibition zones of 11.3 mm at 300 ppm.	Kurniawan et al[38]
10.	*Melastoma malabathricum*/ Melastomataceae	Antidiabetic and Antioxidant	Extract	Methanol	Flavonoids, phenolics, tannins, glucosidase	DPPH, ABTS	Antioxidant activity assessed using the DPPH and ABTS assays yielded IC_{50} values of 8.58 ± 0.03 and 4.59 ± 0.03 µg/mL, respectively. In addition, the methanolic extract of *Melastoma malabathricum* leaves exhibited anti-α-glucosidase activity with an IC_{50} value of 75.25 ± 1.60 µg/mL, whereas acarbose, used as a positive control, showed markedly stronger inhibitory activity with an IC_{50} of 7.67 ± 1.14 µg/mL.	Idris et al[39]
11.	*Curcuma longa*/ Zingiberaceae	Antibacterial	Extract	Methanol, Dichloromethane, Acetone, Ethanol, Water	Tannins, alkaloids, flavonoids, steroids, terpenoids, triterpenoids, saponins	Agar well diffusion	Methanol and ethanol extracts showed the largest inhibition zones among the tested solvents, suggesting stronger antibacterial activity under the experimental conditions	Moulick et al[40]

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12.	*Daemonorops draco*/ Arecaceae	Antibacterial	Isolate	n-Hexane, Dichloromethane, Methanol, Water	Bexarotene, taspine, 2-hydroxy-1-naphthaldehyde isonicotinoyl hydrazone. Fig.	Agar well diffusion	Bexarotene (MIC 0.12–0.16 μg/mL) Taspine (MIC= 0.31–0.39 μg/mL) Hydrazone (MIC= 3.96–3.99 μg/mL)	Apaza Ticona et al[41]
		Wound healing	Isolate	n-Hexane, Dichloromethane, Methanol, Water	Bexarotene, taspine, 2-hydroxy-1-naphthaldehyde isonicotinoyl hydrazone. Fig.	Scratch assay on HaCaT and NIH-3T3 cells (positive control:10% FBS)	Activity (%) compared to FBS 10% Bexarotene (100%) Taspine (75%) Hydrazone (65%)	Apaza Ticona et al[41]
13.	*Cecropia peltata* / Urticaceae	Antidiabetic and Antioxidant	Extract	Methanol	Flavonoids, tannins, flavonolignans, triterpenoids, saponins	In vitro (positive control: acarbose)	IC_{50} = 9.0 to 29.8 μg/mL; acarbose IC_{50} = 5069.72 μg/mL under the same assay conditions	Lora et al[42]
14.	*Ginkgo biloba*/ Ginkgoaceae	Antioxidant	Extract	Ethanol	Flavonoids, terpenoids, phenolic acids	ABTS	Flavonoids and terpenoids enhance the activities of endogenous antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), while concurrently reducing malondialdehyde (MDA) levels.	L. Li et al[43]
15.	*Catharanthus roseus*/ Apocynaceae	Antioxidant	Extract	Methanol	Monoterpenes, alkaloids, vinblastine, vincristine	DPPH and ABTS	Incorporation of *Catharanthus* extract enhanced the radical-scavenging activity of the CS-Ca film against both DPPH and ABTS radicals, with the DPPH scavenging efficiency of the CS–Ag–5% Ca film reaching 83.91%.	Zhuo et al[44]
16.	*Aloe vera*/ Asphodelaceae	Antioxidant	Extract	Methanol	Alkaloids, phenols, flavonoids, saponins, terpenoids	DPPH (standard: ascorbic acid)	All of *Aloe vera* samples collected from different regions exhibited notable biological activity, with activity values ranging from 56 to 80.	S. Kumar et al[45]
17	*Carica papaya*/ Caricaceae	Antioxidant	Fraction	Butanol	Phenolic, flavonoid	DPPH and FRAP (Ferric Reducing Antioxidant Power)	DPPH Inhibition: 97% in young leaves and 96.33% in young seeds • Young leaves: 225 μg/mL • Young seeds: 325 μg/mL • Mature leaves: 375 μg/mL • Mature seeds: 650 μg/mL	S. S. Kumar et al[46]
18.	*Moringa oleifera* / Moringaceae	Antioxidant	Extract	Methanol	Beta-carotene, phenolics, amino acids	DPPH and ABTS	Extraction with 100% methanol yielded an IC_{50} value of 57.27 ± 1.68 in the DPPH assay and an IC_{50} value of 197.00 ± 1.79 in the ABTS assay.	Setiawansyah et al[47]
19.	*Lycopodium serratum*/ Lycopodiaceae	Antidiabetic	Isolate	Methanol, n-Hexane, Dichloromethane, Ethyl acetate	Alkaloids (huperzine), miyoshianol B, 3-O-acetyltogohogenol, serratene	In vitro PTP1B (Protein Tyrosine Phosphatase 1B)	The results of the study showed that serrate-type triterpenoids showed a significant inhibitory effect on protein tyrosine phosphatase 1B (PTP1B), with IC_{50} values of 13.50, 17.65, and 16.64 μM.	M. T. Ha et al[48]

(*Continued*)

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Table 1 (Continued).

No	Scientific Name/Family	Reported Activity	Sample Type	Extraction Solvent	Reported Compounds	Experimental Method	Main Findings	Reference
20.	*Euphorbia hirta*/ Euphorbiaceae	Antioxidant	Extract	Ethyl acetate	Rutin	DPPH, ABTS, Hydrogen peroxide scavenging, nitric oxide scavenging	IC_{50} DPPH = 42.2 μg/mL IC_{50} ABTS = 29.1 μg/mL IC_{50} HOS = 36.5 μg/mL IC_{50} NOS = 43.4 μg/mL	Gautam et al[49]
21.	*Persea americana* / Lauraceae	Antibacterial	Extract	Methanol	Phenolics, flavonoids, tannins, alkaloids, anthocyanins, anthraquinones, triterpenoids, steroids and saponins	Microdilution	MIC = 64–128 μg/mL against the tested bacteria, including *Staphylococcus aureus, Escherichia coli*, and *Pseudomonas aeruginosa*.	Ekom et al[50]
22.	*Artocarpus altilis* / Moraceae	Wound healing	Extract	Methanol	Flavonoids, polyphenols, tannins, saponins	White rat *Rattus norvegicus*	The use of ointment containing breadfruit leaf extract (*Artocarpus Altilis*) can increase the density of collagen fibers during the healing process of excision wounds in white rats (*Rattus norvegicus*) with an extract concentration of 6.25%.	Cahya et al[51]
23.	*Pandanus amaryllifolius* Roxb./ Pandanaceae	Antibacterial	Extract	Ethanol	Alkaloids, saponins, flavonoids, tannins, triterpenoids and steroids	DPPH and ABTS	The IC_{50} values obtained for the DPPH and ABTS assays were 11.96 ± 4.01 μg/mL and 26.18 ± 7.44 μg/mL, respectively. Antibacterial activity, assessed through measurement of the diameter of the inhibition zone (DIZ) and percentage of inhibition (PI), varied among the tested pathogens. At a concentration of 50%, *Escherichia coli* exhibited DIZ and PI values of 16.44 ± 1.21 mm and 66.76 ± 4.92%, respectively, whereas *Staphylococcus aureus* showed higher inhibitory responses, with corresponding values of 21.22 ± 0.11 mm and 82.49 ± 3.91%.	D. K. Wahyuni et al[52]
24.	*Piper betle* L./ Piperaceae	Wound healing	Fraction	n-Hexane, ethyl acetate, methanol	Polyphenols, Betel-phenol, chavicol	In vitro in NIH3T3 cells and in vivo in Swiss mice	In NIH3T3 fibroblast cells, treatment with *Piper betle* leaf extract at concentrations of 2.5 and 5 g resulted in a marked increase in cell proliferation, reaching approximately 2.0- and 1.78-fold, respectively, compared with the control group. Furthermore, scratch assay analysis demonstrated a 1.53-fold enhancement in fibroblast migration. Consistent with the in vitro findings, in vivo evaluation revealed that the percentage of burn wound closure in treated mice reached 32%, 68%, and 80% on days 2, 4, and 6, respectively, whereas control animals exhibited substantially lower healing rates of 20%, 38%, and 43% at the corresponding time points.	Lien et al[53]

25.	*Tinospora cordifolia*/ Menispermaceae	Wound healer	Extract	Methanol	Flavonoids, glycosides, lactones, alkaloids, sterols, saponins, steroids	Wounds in Wistar rats	Excisional wound closure progressed more rapidly in the treated group than in the control group, with healing rates of 94.6% versus 88.9% on day 16 and 99.4% versus 93.6% on day 18, respectively.	Hashilkar et al[54]
26.	*Allium sativum*/ Amaryllidaceae	Antibacterial	Extract	Aqueous solvent	Flavonoids, polyphenols	Disc diffusion	Disc diffusion assays demonstrated that palladium nanoparticle (Pd NP) extracts derived from *Allium sativum* exhibited pronounced antibacterial activity against multidrug-resistant (MDR) bacterial strains, with inhibition zones ranging from 14 to 22 mm. The minimum inhibitory concentrations (MICs) of Pd NPs against the tested MDR bacteria ranged from 3.125 to 50 U/mL. Moreover, co-administration of Pd NPs with conventional antibiotics resulted in a synergistic antibacterial effect. The extract also showed notable bioactivity, with an IC_{50} value of 64.27 μg/mL.	Hamid et al[55]
27.	*Curcuma xanthorrhiza*/ Zingiberaceae	Antioxidants	Extract	Ethanol	Xanthorrhizol, curcumin	DPPH	The ethanolic extract contained 27.0% xanthorrhizol and 7.10% curcumin, and showed antioxidant activity with an IC_{50} value of 64.27 ppm	Kesumayadi et al[56]
		Antibacterial	Extract	Ethanol	Xanthorrhizol, curcumin	Agar dilution	The extract showed antibacterial activity against MRSA (Methicillin-Resistant *Staphylococcus aureus)* ATCC 4330 and MRSA clinical strain 7097, with an MIC value of 5 mg/mL	Kesumayadi et al[56]
		Wound-healing related activity	Extract	Ethanol	Xanthorrhizol, curcumin	In vivo in Wistar rats	Topical gels containing 1%, 3%, and 5% *Curcuma xanthorrhiza* extract were administered twice daily for 12 days in MRSA-infected second-degree burn wound model in rats	Kesumayadi et al[56]
28.	*Chromolaena odorata* L./ Asteraceae	Anti-inflammatory	Fraction	Ethanol	Flavonoids (sinensetin, rhamnetin, tamarixetin, kaempferide), apigenin, terpenoids, alkaloids	Edema in the ears (xylene induction) and feet of mice (carrageenan induction)	30% fraction showed mild inhibitory effect on rat ear edema and paw edema	H. F. Li et al[57]
		Wound healing	Fraction	Ethanol	Flavonoids (sinensetin, rhamnetin, tamarixetin, kaempferide), apigenin, terpenoids, alkaloids	Excision wound on the back skin of a mouse	The 30% fraction at a concentration of 1.0 μg/mL significantly enhanced the rate of cutaneous wound healing in rats, as evidenced on days 3, 6, and 9.	H. F. Li et al[57]
		Antibacterial	Fraction	Ethanol	Flavonoids (sinensetin, rhamnetin, tamarixetin, kaempferide), apigenin, terpenoids, alkaloids	Plate dilution	The 30% fraction demonstrated antibacterial activity against all bacterial strains evaluated.	H. F. Li et al[57]

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Table 1 (Continued).

No	Scientific Name/Family	Reported Activity	Sample Type	Extraction Solvent	Reported Compounds	Experimental Method	Main Findings	Reference
29.	*Azadirachta Indica A.* Juss / Meliaceae	Antioxidant	Extract	Ethanol	Tannins, salicylic acid, flavonoids	ABTS and CUPRAC (Cupric Ion Reducing Antioxidant Capacity)	The IC_{50} value for ABTS radical scavenging activity was 30.02% inhibition, whereas the IC_{50} determined using the CUPRAC assay was 0.918 μg/mL.	Boukeloua et al[58]
30.	*Jatropha multifida* L.	Antioxidant	Extract	Ethanol, Water-ethanol, Methanol. Acetone, Dichloromethane	Phenolic, polyphenol	DPPH, ABTS, FRAP, LPO	Best antioxidant activity: • DPPH (ethanol) IC_{50} = 0.72 ± 0.03 mg/mL • ABTS (ethanol water) = 0.49 ± 0.11 mol ET/g • FRAP (methanol) = 46.23 ± 1.10 μg EAA/g • LPO (Lipid Peroxidation) all extracts effectively reduces lipid peroxidation	Dah-Nouvlessounon et al[59]
		Anti-inflammatory	Extract	Ethanol, water-ethanol, methanol. Acetone, Dichloromethane	Phenolic, polyphenol	Inhibition of albumin denaturation	The water–ethanol extract had the strongest inhibition of albumin denaturation, achieving 97.31 ± 0.35% at a concentration of 1000 μg/mL among the evaluated extracts.	Dah-Nouvlessounon et al[59]
		Antimicrobial	Extract	Ethanol, water-ethanol, methanol. Acetone, Dichloromethane	Phenolic, polyphenol	Disc diffusion	The minimum bactericidal concentration (MBC) against *Staphylococcus aureus* and *Candida albicans* was 22.67 mg/mL, whereas a higher MBC value of 47.61 mg/mL was required for *Escherichia coli*.	Dah-Nouvlessounon et al[59]
31.	*Lannea coromandelica*/ Anacardiaceae	Antibacterial	Extract	Methanol and Aqueous solvent	Alkaloids, flavonoids, steroids, saponins, tannins, glycosides, terpenoids	In vitro agar diffusion method	Among the evaluated extracts, the methanolic extract exhibited the greatest antibacterial activity, producing the largest inhibition zone at a concentration of 15 mg/mL, with inhibition diameters ranging from 2.5 to 7.5 mm.	H. A. Ha et al[60]
32.	*Diplazium esculentum*/ Athyriaceae	Anti-inflammatory	Extract	Ethanol	Saponins, steroids, flavonoids, tannins	Carrageenan-induced male mice	At 360 minutes, the highest percentage of inflammation inhibition was observed with the extract administered at 500 mg/kg body weight, achieving a 92.60% reduction in inflammatory response, which was comparable to that of Voltaren, with no statistically significant difference between treatments ($p > 0.05$).	Zaini et al[61]
33.	*Momordica charantia L.*/ Cucurbitaceae	Anti-inflammatory	Extract	Methanol	Flavonoids, polysaccharides, alkaloids, steroids, triterpenoids	Western blot	*Momordica charantia* has demonstrated the capacity to elevate levels of the anti-inflammatory cytokine interleukin-10 (IL-10), a phenomenon ascribed to its suppression of the NF-κB signaling pathway, a principal regulator of inflammatory responses.	Bai et al[62]

34.	*Salvadora persica* / Salvadoraceae	Anti-inflammatory	Extract	Ethanol	Flavonoids, saponins, tannins, phenolics, terpenes, sterols, alkaloids, glycosides	In vivo Sprague-Dawley rats	A 20% *Salvadora persica* extract was found to promote oral wound healing in mice, an effect correlated with reduced serum levels of inflammatory mediators, such as interleukin-1β, interleukin-6, tumor necrosis factor-α, and transforming growth factor-β1.	Adilah Harun et al[63]
35.	*Anredera cordifolia*/ Basellaceae	Anti-inflammatory	Extract	Ethanol	Terpenoids, steroids, glycosides, flavonoids, saponins, alkaloids	In vivo in mice	The addition of *Anredera cordifolia* leaf extract to celecoxib can accelerate wound healing. This was demonstrated by the reduction in scarring in the group using the mixture compared to celecoxib gel without *Anredera cordifolia extract.*	Istyastono & Yuliani[64]
36.	*Ichnocarpus frutescens*/ Apocynaceae	Antidiabetic	Extract	Petroleum ether, Chloroform, Ethanol and Water	Flavonoids (quercetin) kaempferol-3-glucoside	In vivo in Wistar rats and albino mice	Administration of *Ichnocarpus frutescens* flower extract at a dosage of 500 mg/kg body weight significantly decreased blood glucose levels in diabetic mice.	FP et al[65]
37.	*Bergia ammannioides*/ Elatinaceae	Wound healing	Fraction	n-Hexane, Chloroform, Ethyl acetate, n-butanol	Lupeol, β-Sitosterol, cyclolaudenol, cycloartenol	Sprague-Dawley rats and Swiss albino mice	The 10% ointment containing the n-hexane fraction showed the highest wound closure percentage (85.62%), followed by the ethyl acetate fraction, which attained a healing rate of 81.29%.	Ezzat et al[66]
		Anti-inflammatory	Fraction	n-Hexane, Chloroform, Ethyl acetate, n-butanol	Lupeol, β-Sitosterol, cyclolaudenol, cycloartenol	Edema inhibition	The hexane fraction showed the highest edema inhibition (64.5%) compared to Voltaren. This is in line with the β compound from the hexane fraction showing the highest activity (83.8%).	Ezzat et al[66]
		Antioxidant	Fraction	n-Hexane, Chloroform, Ethyl acetate, n-butanol	Lupeol, β-Sitosterol, cyclolaudenol, cycloartenol	DPPH and ABTS	The ethyl acetate fraction exhibited the most potent free radical scavenging activity among the evaluated fractionation: • DPPH: IC_{50} = 10.25 µg/mL • ABTS: IC_{50} = 66.09 µg/mL	Ezzat et al[66]
		Antibacterial	Fraction	n-Hexane, Chloroform, Ethyl acetate, n-butanol	Lupeol, β-Sitosterol, cyclolaudenol, cycloartenol	Disc diffusion	The hexane fraction exhibited the highest antibacterial activity against *Staphylococcus aureus*, with a minimum inhibitory concentration (MIC) of 104 µg/mL.	Ezzat et al[66]
38.	*Clibadium surinamense*/ Asteraceae	Antioxidant	Extract	Aqueous solvent	Phenolic	DPPH, FRAP, TEAC (Trolox Equivalent Antioxidant Capacity)	Antioxidant activity was evaluated using the DPPH, FRAP and TEAC assays, yielding values of 940 ± 41.0, 820 ± 75.0, and 1410 ± 82.7 µmol TE/g, respectively.	Jiménez et al[67]

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Table 1 (Continued).

No	Scientific Name/Family	Reported Activity	Sample Type	Extraction Solvent	Reported Compounds	Experimental Method	Main Findings	Reference
39.	*Croton bonplandianum*/ Euphorbiaceae	Antibacterial	Extract	Ethyl Acetate, Benzene, Chloroform, Methanol and n-Hexane	Alkaloids, saponins, flavonoids, proteins and tannins	Agar diffusion	The ethyl acetate extract at a concentration of 300 mg/mL had the most potent antibacterial effect, yielding the largest inhibition zone against *Salmonella enterica* (20.6 ± 1 mm), whereas a smaller zone of inhibition was observed against *Staphylococcus haemolyticus* (18.0 ± 1 mm).	Ghosh[68]
40.	*Imperata cylindrica* (L.) Raeusch/ Poaceae	Anti-inflammatory	Extract	Ethanol	Flavonoids, alkaloids, tannins, steroids and terpenoids	LPS	The ethanolic extract of *Imperata cylindrica* (L.) Raeusch at a concentration of 640 ppm was found to reduce nitric oxide secretion in fibroblast cells.	Mangkulion et al[69]

Abbreviations: ABTS, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid); CAT, catalase; CUPRAC, cupric ion reducing antioxidant capacity; DPPH, 2,2-diphenyl-1-picrylhydrazyl; FBS, fetal bovine serum; FRAP, ferric reducing antioxidant power; GFAP, glial fibrillary acidic protein; GSH, glutathione; IC50, half-maximal inhibitory concentration; IL, interleukin; LPO, lipid peroxidation; LPS, lipopolysaccharide; MBC, minimum bactericidal concentration; MDA, malondialdehyde; MDR, multidrug-resistant; MIC, minimum inhibitory concentration; MRSA, methicillin-resistant Staphylococcus aureus; NF-κB, nuclear factor kappa B; pNPG, p-nitrophenyl-B-D-glucopyranoside; PTP1B, protein tyrosine phosphatase 1B; SOD, superoxide dismutase; TEAC, Trolox equivalent antioxidant capacity.

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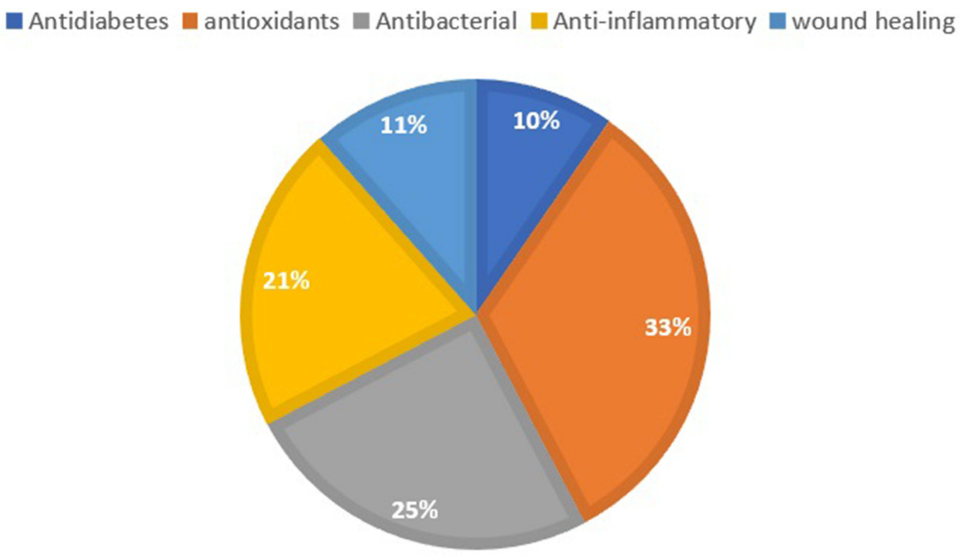

Figure 1 Distribution of reported pharmacological activities among 40 medicinal plants used by the Anak Dalam tribe and evaluated for their relevance to diabetic wound-healing research. The percentages indicate the frequency of reported pharmacological activities across the reviewed studies and should not be interpreted as measures of comparative efficacy or clinical effectiveness.

various plant parts such as roots, leaves, shoots, bark, and stems. Typically, these materials are prepared using simple techniques, including decoction, maceration, topical application, or oral administration.[27] To date, the majority of these medicinal plants have been investigated predominantly in vitro. Nevertheless, in vivo evidence supporting wound-healing efficacy has been reported for *Artocarpus altilis, Piper betle, Ichnocarpus frutescens*, and *Bergia ammannioides*. As summarized in Table 1, these studies demonstrate tangible effects such as enhanced wound contraction, increased collagen deposition, and accelerated re-epithelialization.

According to Table 1, ethanol was the most commonly used extraction solvent. Lee et al[70] assert that ethanol is generally regarded as a universal solvent for the extraction of natural products due to its extensive solubility profile. It could efficiently extract hydrophilic and lipophilic components, including phenolic and flavonoid compounds. Correspondingly, ethanol is considered a safe and acceptable solvent for pharmaceutical purposes, thereby offering significant advantages over other organic solvents like methanol.[71]

Goniothalamus macrophyllus (see Table 1) is a traditional medicine commonly used by the Anak Dalam tribe for wound management. The bark of the plant is usually processed by pounding and squeezing to obtain an extract, which is then applied topically to the injured area.[26] Appropriately, experimental studies have scientifically validated that the bioactive compounds of this plant demonstrate antibacterial activity. This evidence supports the empirical application of *G. macrophyllus* by local communities for wound healing and infection prevention.[72]

Additionally, the leaves of plants such as *Clibadium surinamense* (Table 1) are traditionally utilized by chewing and subsequently applying the material to injuries. According to local ethnomedical practices, this application is traditionally intended to promote hemostasis and support wound healing. Unquestionably, scientific evidence supporting this specific practice remains limited.

Daemonorops draco, known locally as "Rotan Darah Naga" (Table 1), has been traditionally utilized in wound treatment due to the bioactive properties of its resin. This resin is reported to possess significant antibacterial capabilities and a notable ability to facilitate the healing process. Conventionally, the Anak Dalam tribe combines the resin with turmeric and gently heats it over hot coals until it emits a characteristic odor. This scent is likely associated with its volatile phytochemical constituents. The heating process continues until the mixture attains a soft, semi-solid consistency that simplifies topical application. Subsequently, the mixture is applied directly to the wound as part of traditional practices intended to promote hemostasis, reduce infection risks, and support skin repair. This specific method has been transmitted across generations within the Anak Dalam community in Jambi Province as a vital part of their ethnomedical heritage.[73]

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The Anak Dalam tribe in Jambi Province also utilizes *Imperata cylindrica* (L.) Raeusch., commonly known as "alang-alang" (Table 1), as a traditional wound-healing agent. Within their ethnomedical practice, fresh roots of *I. cylindrica* are pounded to obtain a smooth paste. Resultantly, this paste is mixed with vegetable oils (eg, palm oil) and applied to the injured area. This preparation is traditionally used to promote hemostasis, reduce inflammation, and accelerate the overall healing process.[73]

According to Yolandari et al, the medicinal plants used by the Anak Dalam tribe in Jambi are rooted in empirical experience and cultural beliefs. These spiritual values have been passed down through generations. Specifically, most traditional knowledge is obtained through dreams and communication with spiritual ancestors, such as *Dewa* and *Datuk*. The community believes that plants possess a soul or an inherent natural power. Ordinarily, traditional healing practices involve rituals, mantras, and prayers to these spiritual ancestors to enhance the effectiveness of the treatment.[74]

The ethnobotanical information supporting this discussion was derived from previously published studies and field-based documentation describing these traditional healing practices. According to the Anak Dalam beliefs, treatment effectiveness depends on strict obedience to rituals and taboos. These practices are understood to balance the human body, nature, and the spiritual forces that support recovery. Simultaneously, traditional medicinal knowledge involving plant species rich in phytochemical compounds (eg, alkaloids, flavonoids, tannins, and terpenoids) provides a physiological basis for healing. These compounds act as antioxidants, antibacterials, and anti-inflammatories, which are believed to accelerate wound drying and prevent infection.

Admittedly, while 40 medicinal plants have been identified, the majority of these species have not been specifically evaluated using diabetic wound-healing models. Consequently, a collaboration among indigenous communities, researchers, and the government is essential to preserve this traditional knowledge. Furthermore, such partnerships are necessary to validate these practices through systematic and scientifically rigorous approaches.

Discussion

Diabetic wound healing is a complex pathological process defined by persistent hyperglycemia, excessive oxidative stress, chronic inflammation, and impaired angiogenesis. These factors, alongside an increased susceptibility to infection, collectively contribute to significantly delayed tissue repair.[75] Notably, medicinal plants traditionally utilized by the Anak Dalam tribe contain a diverse array of bioactive compounds, such as flavonoids, alkaloids, and terpenoids. Preclinical studies indicate that these secondary metabolites effectively modulate pathological processes by targeting multiple biological pathways. Specifically, these compounds are reported to reduce oxidative stress, inhibit pro-inflammatory signaling pathways, and exert potent antibacterial effects against common wound pathogens.[76] Through these proposed multi-target mechanisms, the Anak Dalam medicinal plants may synergistically promote essential phases of wound recovery. These phases include fibroblast proliferation, collagen synthesis, and re-epithelialization. Nevertheless, these mechanistic links are largely inferred from preclinical and indirect pharmacological investigations. Consequently, such findings should not be interpreted as definitive evidence of clinical efficacy in the treatment of diabetic ulcers.

Phytochemical Constituents Related to Antidiabetic Wound Healing

This section analyzes the phytochemical constituents reported in medicinal plants used by the Anak Dalam tribe alongside their potential relevance to diabetic wound-healing mechanisms. Specifically, the discussion focuses on primary compound classes, suggested mechanisms of action, and the strength of available preclinical evidence. Chronic hyperglycemia leads to heightened oxidative stress and increased matrix metalloproteinase (MMP) activity. Distinctively, these factors inhibit fibroblast proliferation, impair angiogenesis, and facilitate extracellular matrix degradation, thereby delaying essential repair processes.[77] Moreover, chronic wounds in patients with diabetes mellitus are often linked to vascular dysfunction, peripheral neuropathy, and immunological dysregulation. Collectively, these conditions impair tissue repair and delay the critical phase of re-epithelialization.[78] Within this pathological context, phytochemical compounds are reported to modulate inflammatory responses, oxidative stress, and tissue remodeling pathways in experimental models. Such interactions suggest a significant potential relevance to wound-healing processes. Paradoxically, most of the supporting evidence is derived from animal models. Strict caution is required when extrapolating these findings to humans due to fundamental differences in skin structure and healing mechanisms between species.[79]

A literature review of medicinal plants traditionally used by the Anak Dalam tribe in Jambi Province reveals a diverse array of bioactive compounds, including flavonoids, alkaloids, saponins, tannins, and terpenoids. These substances hold potential relevance to chronic diabetic wound management. Generally, these compounds are recognized for biological activities such as free radical scavenging and antimicrobial properties. These traits are essential in alleviating oxidative stress and preventing infection during the recovery period.[80] To provide a more systematic understanding, the relationship between bioactive compounds and the different stages of wound healing is summarized in Table 2.

As summarized in Table 2, bioactive compounds derived from medicinal plants used by the Anak Dalam community contribute to different stages of the wound-healing process through distinct yet interconnected mechanisms. Ordinarily, several compounds exhibit pleiotropic effects and act across multiple recovery phases. This suggests a multi-target biological relevance within the complex pathological environment typical of diabetic wounds.

Flavonoid compounds associated with wound-healing processes are found in various medicinal plants traditionally utilized by the Anak Dalam tribe, including *Syzygium myrtifolium, Centella asiatica, Zingiber cassumunar, Kaempferia galanga*, and *Tinospora cordifolia*. These plant materials are typically prepared by decoction. Effectively, this technique facilitates the extraction of bioactive compounds and promotes rapid bioavailability upon consumption.[88] Furthermore, the antioxidant and anti-inflammatory activities of flavonoids are significantly influenced by the quantity and positional distribution of hydroxyl groups on the A and B aromatic rings. Logically, these chemical structures are crucial in determining the overall biological efficacy of the plant extract.[89]

Unquestionably, several studies have shown that alkaloids contribute to wound closure and promote extracellular matrix synthesis during the healing of diabetic injuries.[90] The Anak Dalam tribe traditionally utilizes medicinal herbs containing these alkaloids, such as *Croton bonplandianum, Anredera cordifolia, Lannea coromandelica*, and *Tinospora cordifolia*. In vivo studies have demonstrated that alkaloid-rich extracts accelerate wound contraction and enhance the deposition of collagen types I and III. Specifically, these substances stimulate epidermal thickening and elevate the expression of proliferating cell nuclear antigen (PCNA), which serves as a critical marker of cellular proliferation.[91]

Asiaticoside (a terpenoid saponin compound derived from *Centella asiatica*) is extensively documented to exhibit wound-healing activity in diabetic conditions.[85,92,93] Generally, asiaticoside demonstrates antioxidant properties that mitigate oxidative stress. This protective effect effectively prevents further tissue damage during the recovery phase.[93] Furthermore, this compound is shown to stimulate angiogenesis through the upregulation of vascular endothelial growth factor (VEGF),

Table 2 Proposed Mechanisms of Bioactive Compounds in Diabetic Wound Healing

Wound Healing Phase	Bioactive Compounds	Activities and Proposed Mechanisms in Diabetic Wounds	References
Hemostasis	Tannins	Exhibit astringent properties by precipitating proteins, promoting vasoconstriction, and facilitating early clot formation, thereby reducing bleeding and supporting initial wound sealing	[81]
Inflammation	Flavonoids (Quercetin, Resveratrol), Alkaloids, Curcumin	Suppress excessive inflammatory response by inhibiting NF-κB signaling pathway, reducing pro-inflammatory cytokines (TNF-α, IL-1β, IL-6), and promoting macrophage polarization from M1 to M2 phenotype. Also exhibit antioxidant activity by scavenging ROS	[82–84]
Proliferation	Flavonoids, Terpenoids (asiaticoside), Saponins	Promote fibroblast proliferation, collagen synthesis, angiogenesis (via VEGF upregulation), and keratinocyte migration. Enhance extracellular matrix (ECM) formation	[13,85,86]
Remodeling	Flavonoids, Triterpenoids, Polyphenols	Regulate collagen remodeling by balancing MMPs and TIMPs, enhance collagen cross-linking, and improve tensile strength of healed tissue while minimizing scar formation	[13,87]

Abbreviations: ECM, extracellular matrix; IL, interleukin; MMPs, matrix metalloproteinases; NF-KB, nuclear factor kappa B; ROS, reactive oxygen species; TIMPs, tissue inhibitors of metalloproteinases; TNF-a, tumor necrosis factor-alpha; VEGF, vascular endothelial growth factor.

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cluster of differentiation 34 (CD34), inducible nitric oxide synthase (iNOS), and endothelial nitric oxide synthase (eNOS). Collectively, these molecular changes facilitate neovascularization and accelerate wound closure in diabetic models.[92]

Several experimental studies suggest that interactions among phytochemical constituents significantly enhance biological activities relevant to diabetic recovery. In a diabetic mouse model, the combined administration of allicin and quercetin was demonstrated to enhance the expression of essential growth factors, including transforming growth factor-beta (TGF-β) and VEGF. Correspondingly, this combination reduced levels of the proinflammatory cytokine tumor necrosis factor-alpha (TNF-α). These results showed improved healing outcomes compared with the administration of each compound separately.[94] Additionally, in vitro studies indicate that combining quercetin and curcuminoids demonstrates significant antioxidant activity. As evidenced by DPPH and ABTS assays, such combinations likely possess potent anti-inflammatory properties.[95]

Ultimately, the bioactive compounds reported in medicinal plants traditionally used by the Anak Dalam tribe are associated with several critical pharmacological activities. These include the augmentation of collagen synthesis, the protection of sensitive tissues against microbial infections, and the promotion of overall tissue repair. The principal mechanisms through which these compounds are proposed to support the wound-healing process are summarized in the subsequent mechanistic framework.

Regulation of Blood Sugar Levels

The onset of diabetes is associated with insulin resistance and β-cell dysfunction, as reflected by alterations in homeostatic model assessment indices for insulin resistance (HOMA-IR) and β-cell function (HOMA-β).[96] Unquestionably, these changes may be accompanied by structural alterations in hepatocytes and pancreatic islets. Such shifts are often linked to the increased expression of intestinal glucose transporters, such as sodium-glucose cotransporter 1 (SGLT1) and glucose transporter 2 (GLUT2).[97] These transporters play vital roles in intestinal glucose sensing by mediating the glucose-stimulated secretion of incretin hormones, such as glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1). Correspondingly, these hormones are crucial for maintaining glucose homeostasis.[98]

Plant-derived natural compounds are reported to modulate glucose regulation effectively, with flavonoids representing a major class of bioactive molecules.[99] Particularly, flavonoids present in cinnamon extracts (procyanidin and epicatechin derivatives) may influence intestinal glucose transport by downregulating GLUT2 expression. This specific transporter is key for transferring glucose from the intestinal lumen into the systemic circulation.[100] Notably, GLUT2 is predominantly localized on the basolateral membrane of enterocytes and facilitates glucose diffusion into the bloodstream.[101] Resultantly, the modulation of GLUT2 activity by these compounds contributes to improved glycemic control. This regulation is an essential factor in supporting successful wound healing under diabetic conditions. A schematic representation of this mechanism is presented in Figure 2

Enhancement of Blood Circulation

In individuals with diabetes mellitus, sustained hyperglycemia can significantly impair peripheral blood circulation. This deterioration typically occurs due to neuropathic changes, reduced cutaneous cellular function, and an elevated risk of atherosclerosis. Substantially, these vascular complications prolong the wound-healing process by restricting the delivery of vital repair factors.[78,102] Accordingly, bioactive compounds exhibiting vasodilatory effects through specific molecular mechanisms are necessary to restore proper blood flow to the affected areas. Various natural compounds, including flavonoids, ginkgolides, and bilobalide, have demonstrated the ability to promote vasodilation through the activation of endothelial nitric oxide synthase (eNOS). This activation leads to increased nitric oxide (NO) production. Paradoxically, these compounds also inhibit extracellular Ca^{2+} influx and Ca^{2+} release from the endoplasmic reticulum. This dual action ultimately induces vascular relaxation.[103–105] Incidental to this relaxation, enhanced blood flow significantly improves the supply of oxygen and nutrients to injured tissues. Resultantly, this improved microcirculation promotes and accelerates the fundamental stages of tissue repair and regeneration.[106] Figure 3 illustrates the specific mechanism by which natural compounds enhance blood circulation.

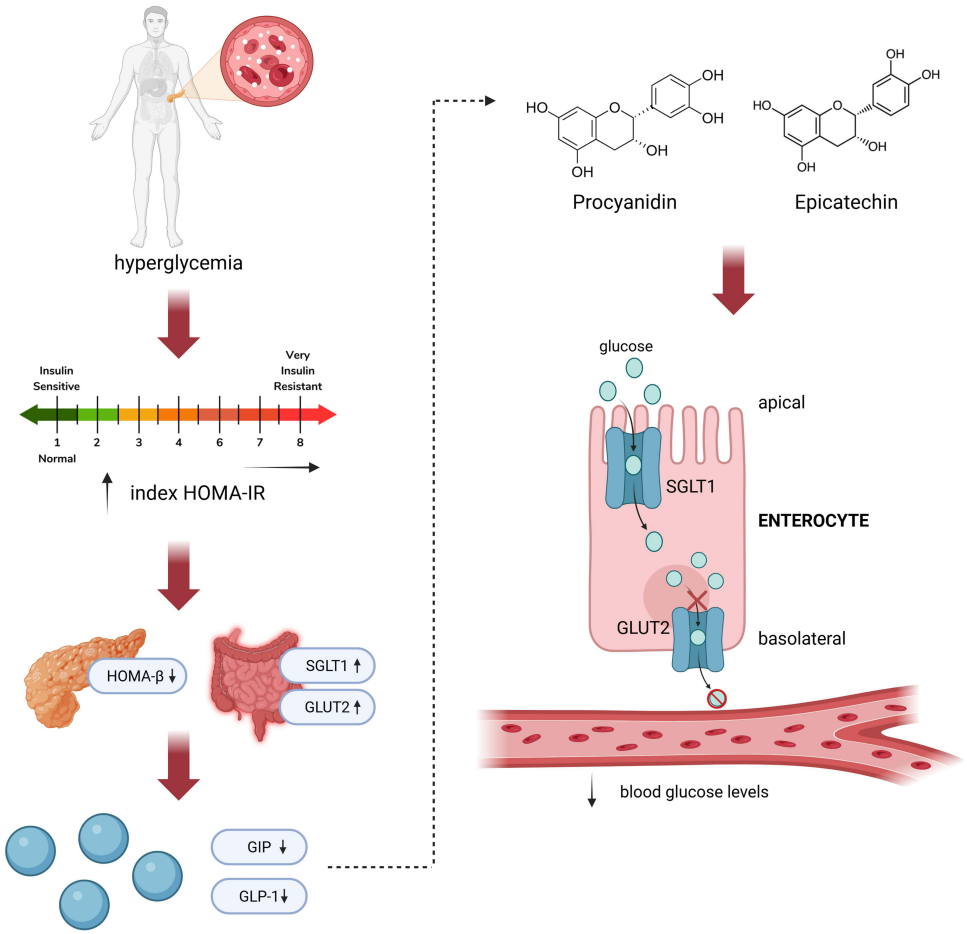

Figure 2 Proposed mechanism of procyanidin and epicatechin compounds in reducing blood glucose levels. Hyperglycemia is associated with increased HOMA-IR, reduced β-cell function (HOMA-β), decreased levels of incretin hormones (GIP and GLP-1), and upregulation of SGLT1 and GLUT2 in the intestine. Procyanidin and epicatechin are suggested to decrease GLUT2 expression, thereby reducing glucose transport into the bloodstream and helping to restore metabolic balance. Arrows indicate the direction of biological effects: upward arrows (↑) represent increased expression or activity, while downward arrows (↓) indicate decreased expression or activity.

Acceleration of New Tissue Formation

The wound-healing process proceeds through four interrelated phases, namely hemostasis, inflammation, proliferation, and remodeling.[107] Natural compounds (eg, polyphenols, terpenoids, alkaloids, saponins, and essential oils) are extensively documented for their substantial involvement in accelerating repair by modulating several of these stages.[108] During the inflammatory phase, flavonoids like quercetin and kaempferol demonstrate a notable ability to downregulate proinflammatory cytokines, such as TNF-α, IL-1β, and IL-6. Correspondingly, these compounds inhibit the activation of the NF-κB signaling pathway. This action attenuates excessive inflammatory responses and establishes a conducive microenvironment for tissue regeneration.[109,110] Progressively, during the proliferative phase, bioactive compounds (eg, asiaticoside derived from *Centella asiatica*) promote extracellular matrix formation. This includes increasing fibronectin expression and enhancing collagen synthesis, which contributes to greater tensile strength.[111] Furthermore, asiaticoside promotes angiogenesis through the upregulation of VEGF expression. This stimulation effectively encourages granulation tissue formation and re-epithelialization.[92,112] Subsequently, during the remodeling phase, polyphenolic compounds exhibit strong antioxidant activity that regulates oxidative stress. These substances promote collagen cross-linking and enhance tissue durability by modulating matrix metalloproteinases (MMPs) and their endogenous inhibitors (TIMPs).[113,114] Inevitably, the anti-inflammatory, pro-proliferative, and remodeling-promoting properties of these natural compounds work together to improve tissue repair in diabetic wounds. Experimental studies consistently show enhanced re-epithelialization and collagen density as a result of these interactions.[115,116] The process of new tissue formation across the different phases of wound healing is illustrated in Figure 4.

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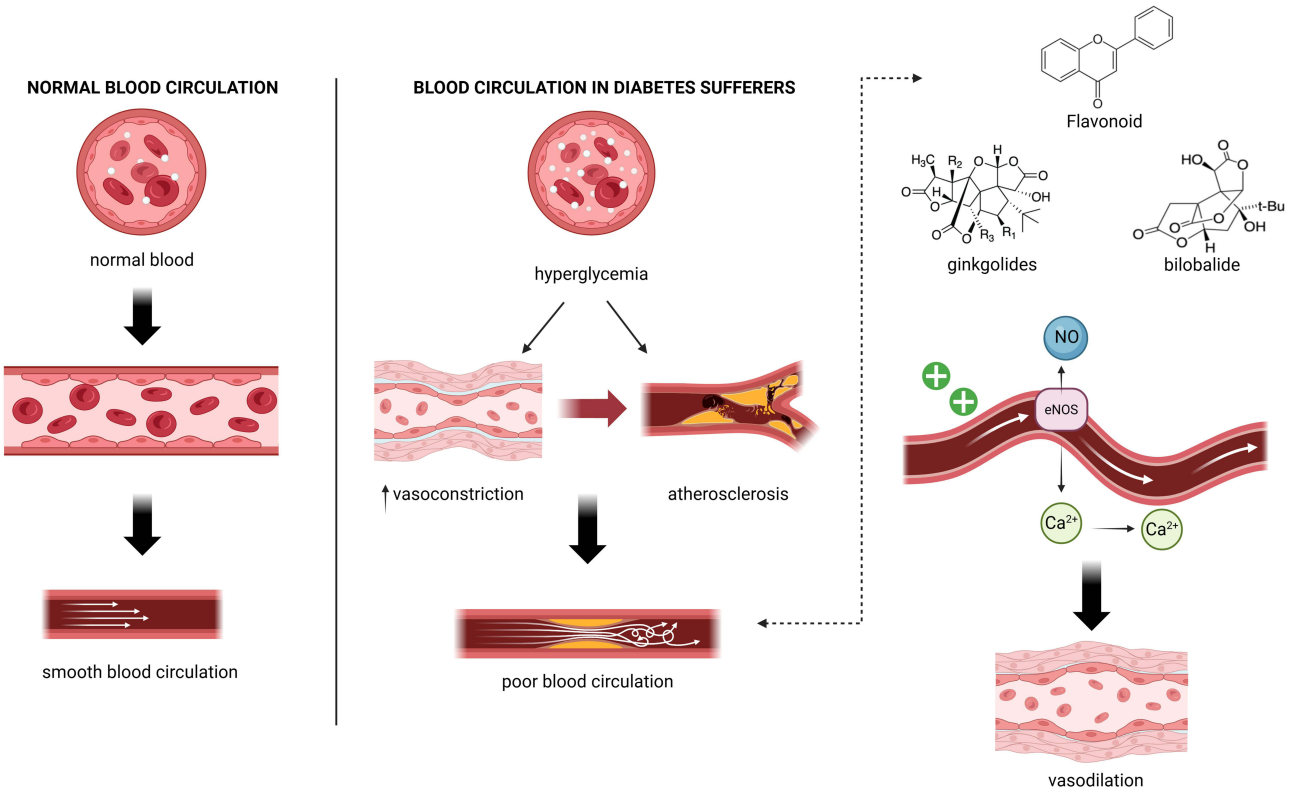

Figure 3 Proposed mechanism of natural compounds in improving blood circulation. These compounds may enhance endothelial nitric oxide synthase (eNOS)-mediated production of nitric oxide (NO) and modulate calcium signaling, thereby promoting vasodilation and improving tissue perfusion in experimental models.

Reduction of Infection and Inflammation

Natural compounds contribute significantly to the wound-healing process by exerting antibacterial actions that lower infection risks. Simultaneously, these substances modulate inflammatory responses through specific anti-inflammatory mechanisms. Bacterial colonization can severely interfere with normal healing by prolonging inflammation and impairing tissue repair.[117,118] Pathogenic microorganisms (eg, *Staphylococcus aureus* and *Pseudomonas aeruginosa*) frequently develop biofilms that facilitate chronic and severe infections.[119] Numerous medicinal plants traditionally used for wound management demonstrate substantial antibacterial activity. For instance, alkaloids exert antibacterial effects by disrupting bacterial membrane integrity. Effectively, these compounds damage cellular structures, interfere with DNA function, inhibit protein activity, and suppress vital metabolic processes.[120–122] Notably, these effects are primarily observed in planktonic bacteria. Their effectiveness against established biofilms may be limited.

Compounds such as quercetin, catechins, alkaloids, and lupeol are reported to exhibit strong anti-inflammatory activity. This occurs partly through the inhibition of critical signaling pathways, including NF-κB, activator protein-1 (AP-1), and mitogen-activated protein kinase (MAPK).[123,124] These interactions result in the suppression of proinflammatory mediators, including TNF-α, IL-1β, iNOS, and COX-2. Substantially, these mediators are recognized for aggravating tissue damage during wound progression.[125] Furthermore, a comprehensive review indicates that alkaloids and terpenoids can inhibit cyclooxygenase (COX) and lipoxygenase (LOX) enzymes. Resultantly, this inhibition reduces the synthesis of inflammatory mediators and contributes to pain alleviation.[126] The antibacterial and anti-inflammatory mechanisms involved in wound healing are illustrated in Figure 5.

Protection Against Oxidative Stress–Induced Cellular Damage

Natural compounds play vital roles in protecting against cellular damage induced by oxidative stress. This damage typically results from an imbalance between reactive oxygen species (ROS) and the body's endogenous defense systems. Effectively, these compounds operate partly through the activation of nuclear factor erythroid 2-related factor

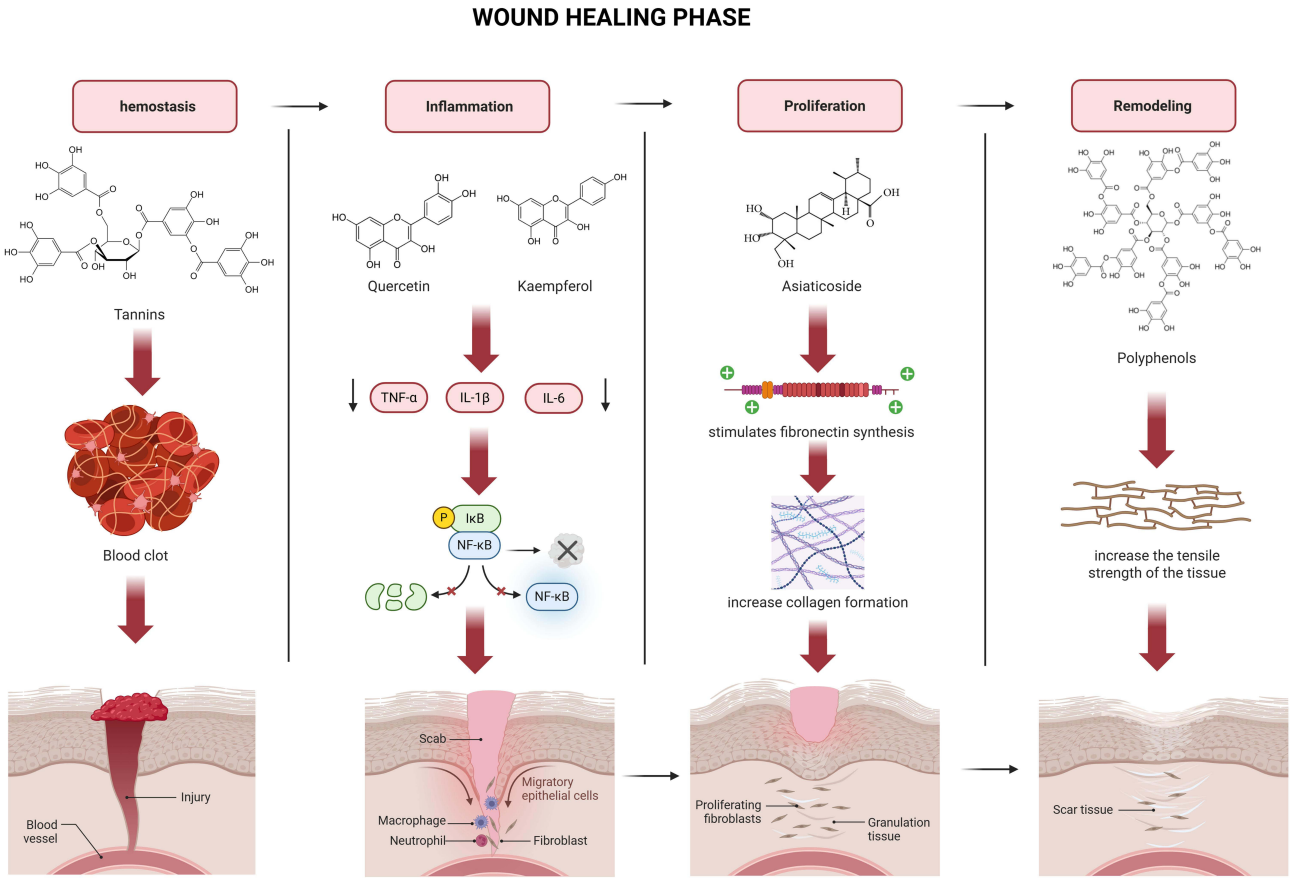

Figure 4 Proposed mechanism of natural compounds in new tissue formation. Bioactive compounds such as tannins, quercetin, kaempferol, asiaticoside, and polyphenols may support wound healing by promoting processes such as fibroblast proliferation, extracellular matrix formation, collagen synthesis, angiogenesis, and re-epithelialization, primarily based on preclinical evidence.

2 (Nrf2) and its downstream target (ie, heme oxygenase-1 (HO-1)). Both are essential components of a broader antioxidant defense network.[127,128] Bioactive substances (ie, quercetin, resveratrol, and saponins) provide cellular protection by neutralizing ROS. Concurrently, they enhance the function of endogenous antioxidant enzymes such as superoxide dismutase (SOD), catalase, and glutathione peroxidase. Explicitly, these strategies successfully impede lipid peroxidation processes that would otherwise compromise essential biomolecules like proteins and DNA.[108,129,130] Figure 6 illustrates the mechanism by which quercetin, resveratrol, and saponin compounds safeguard cells against oxidative stress damage.

The synergistic interactions among several phytochemical components in medicinal plants significantly boost the effectiveness of diabetic wound management. Combinations of bioactive compounds (eg, flavonoids, alkaloids, tannins, and terpenoids) act in concert to address multiple barriers to healing. Persuasively, these constituents are reported to enhance re-epithelialization, stimulate collagen synthesis, and optimize oxidative balance within wound tissues more effectively than singular compounds used in isolation.[131]

Admittedly, a significant challenge in phytochemical research on Anak Dalam plants remains the heterogeneity in compound composition. This variability arises from changes in environmental conditions, extraction methods, and inconsistencies in bioactivity evaluation. Therefore, stringent standardization and comprehensive characterization of active components are crucial. Rigorously, these steps are required to guarantee the reproducibility and consistency of therapeutic outcomes in future medical applications.

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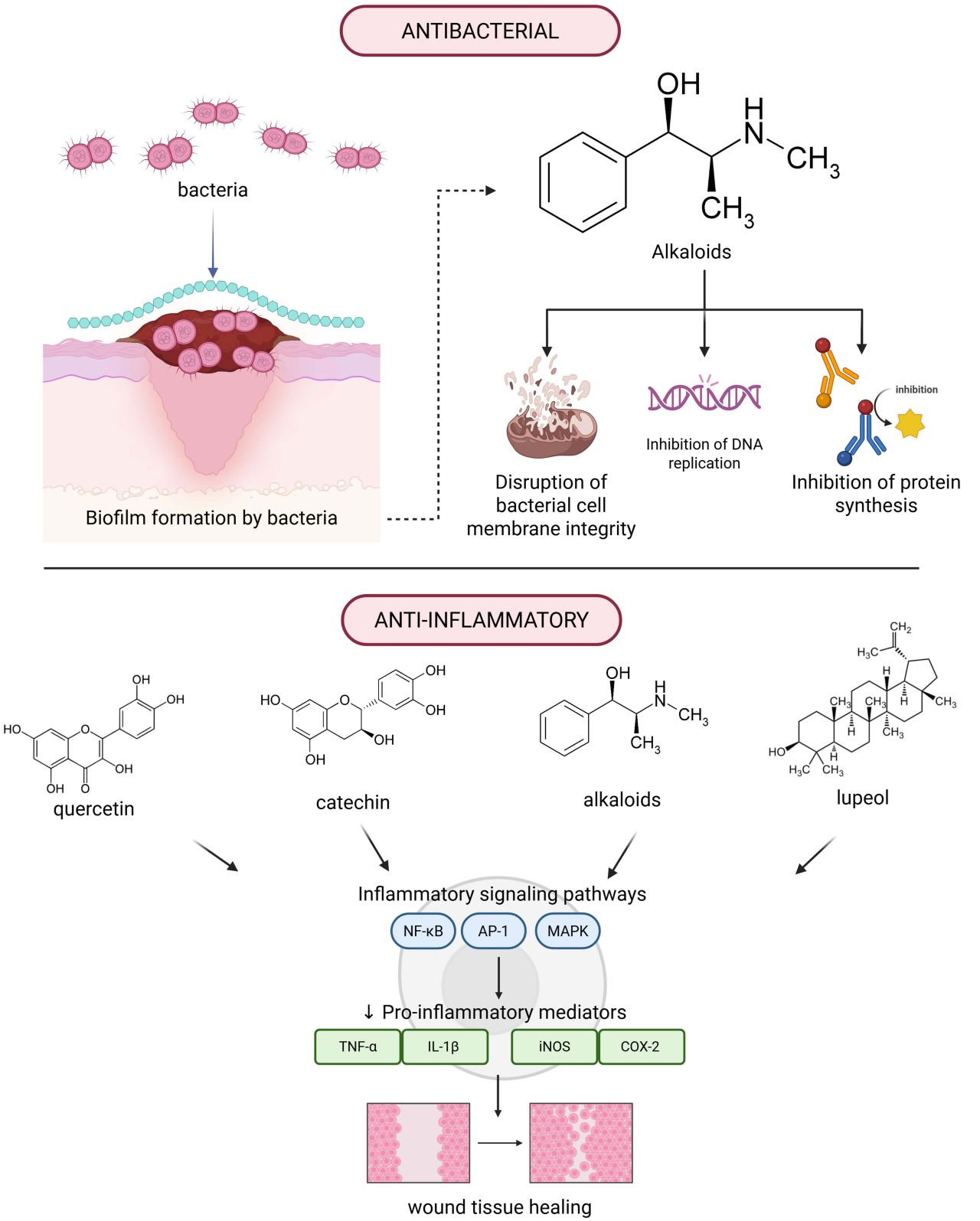

Figure 5 Proposed antibacterial and anti-inflammatory mechanisms of bioactive compounds in wound healing. Bioactive compounds exert antibacterial effects by disrupting bacterial cell membrane integrity, inhibiting DNA replication, and suppressing protein synthesis, thereby preventing microbial growth and biofilm formation. They also exhibit anti-inflammatory activity by modulating NF-κB, AP-1, and MAPK signaling pathways, leading to decreased expression of pro-inflammatory mediators such as TNF-α, IL-1β, IL-6, iNOS, and COX-2. These mechanisms are primarily supported by preclinical and mechanistic evidence.

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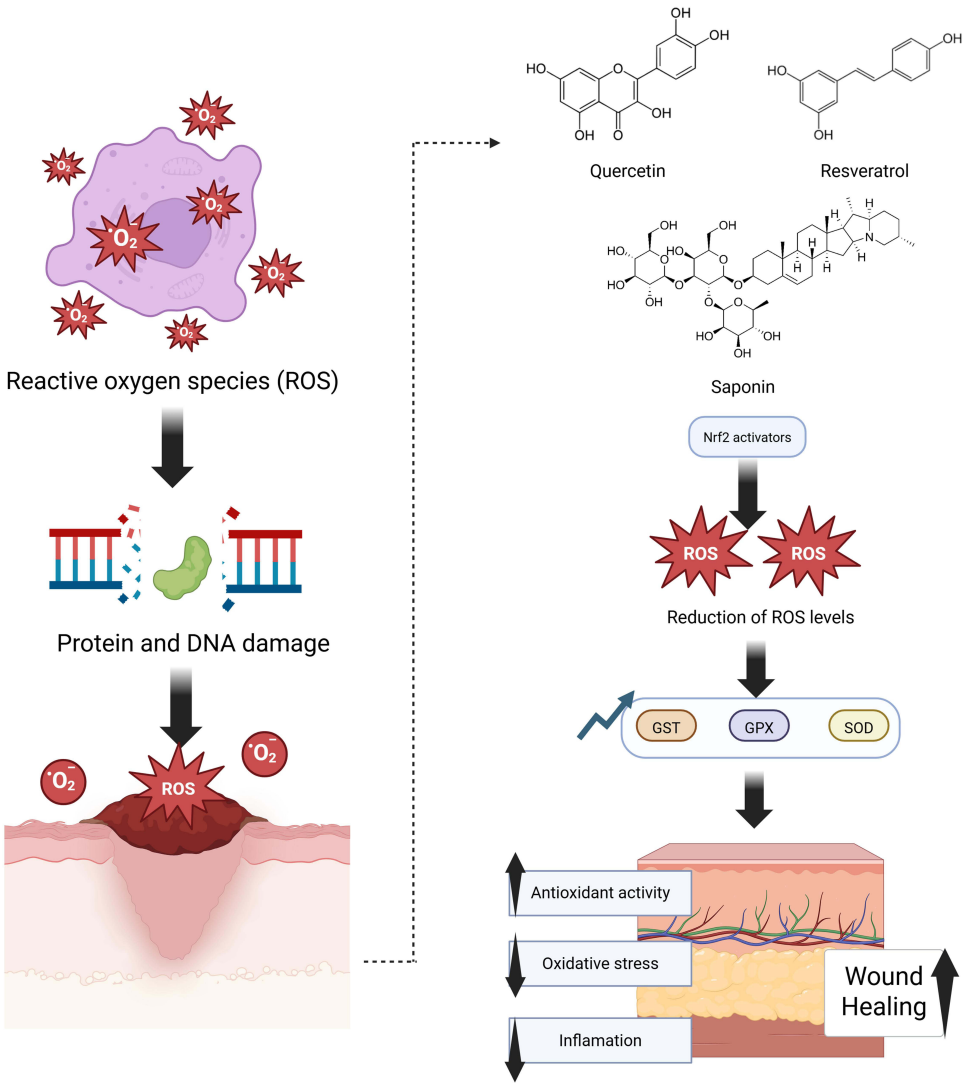

Figure 6 Proposed mechanisms of natural compounds in protecting cells from oxidative stress-induced damage. Reactive oxygen species (ROS), including O_2^-, cause protein and DNA damage that impairs wound healing. Bioactive compounds such as quercetin, resveratrol, and saponins activate Nrf2 signaling, leading to the upregulation of antioxidant enzymes (GST, GPx, and SOD). This process reduces ROS levels, oxidative stress, and inflammation, thereby promoting tissue repair and wound healing. Arrows indicate activation, while downward arrows indicate reduction.

Pharmacological Evidence Relevant to Wound-Healing Mechanisms

Pharmacological evidence is vital for evaluating the biological relevance and translational potential of medicinal plants traditionally used for wound-related conditions. In vitro, in vivo, and clinical studies are essential for assessing the efficacy, safety, and therapeutic possibilities of phytochemical compounds in managing diabetic wounds. Curiously, in the context of the medicinal plants reviewed here, most available evidence remains preclinical or indirect. Therefore, these findings cannot yet establish definitive therapeutic efficacy for patients suffering from diabetic ulcers.

Syzygium myrtifolium Walp

Syzygium myrtifolium, locally known as "pucuk merah," is a medicinal plant traditionally employed by the Anak Dalam tribe. It is a shrub or small tree belonging to the angiosperm family Myrtaceae. Geographically, the species is extensively dispersed throughout South and Southeast Asia, encompassing Myanmar, Thailand, Indonesia, Malaysia, the Philippines, and Singapore.[30]

Specifically, *Syzygium myrtifolium* is typically found near roadsides and is frequently cultivated as an ornamental species.[132] *Pucuk merah* has been utilized in traditional medicine to mitigate gastrointestinal distress, particularly

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stomach pain.[133] Phytochemical analyses indicate that *pucuk merah* contains a variety of secondary metabolites, including alkaloids, flavonoids, phenolic compounds, saponins, tannins, and triterpenoids.[30] Appropriately, these bioactive constituents are linked to multiple pharmacological activities, such as antidiabetic,[28] antioxidant,[134] antibacterial,[135] and anti-inflammatory effects.[136]

Based on the findings reported by Vonia et al, acarbose demonstrated an α-glucosidase inhibitory activity of 42.73 ± 0.12% at a concentration of 180 μg/mL. This activity increased to 66.03 ± 1.11% at 200 μg/mL.[137] Notably, these results were compared with a study by Nor et al that assessed the α-glucosidase inhibitory activity of *Syzygium myrtifolium*. At a concentration of 100 μg/mL, the *S. myrtifolium* extract exhibited an inhibitory activity of 50.83 ± 1.27%. Interestingly, this value was not statistically different from that of acarbose ($p > 0.05$). At a concentration of 200 μg/mL, the inhibitory activity of the extract increased to 62.33 ± 3.11%, although it remained slightly lower than the level observed for acarbose.[28] Accordingly, these findings collectively suggest that *Syzygium myrtifolium* possesses α-glucosidase inhibitory activity under the tested experimental conditions. Nevertheless, further clinical studies are required to determine its true relevance to human diabetes management.

A comprehensive study conducted by Abdulrahman evaluated the free radical scavenging activity of ethanol, methanol, and aqueous extracts obtained from the leaves, bark, and roots of *Syzygium myrtifolium*.[29] Using the DPPH assay at a concentration of 100 μg/mL, the study utilized inhibition percentages and IC_{50} values as key parameters. Remarkably, the ethanol extract of the leaves showed the most significant antioxidant activity among all investigated materials. It achieved 89.94% inhibition with an IC_{50} value of 11.87 μg/mL, indicating a powerful capacity to neutralize free radicals. Quercetin served as a reference compound in this study, exhibiting 87.87% inhibition with an IC_{50} of 13.13 μg/mL.[29] Unquestionably, these findings indicate that the ethanolic leaf extract of *S. myrtifolium* demonstrates marginally greater antioxidant efficacy compared to quercetin under the evaluated conditions.

Additionally, the antibacterial activity of *Syzygium myrtifolium* was evaluated using disk diffusion and agar well diffusion assays. Interestingly, both methods yielded comparable results. Inhibition zones ranged from 2.0 to 2.78 mm, with the aqueous extract exhibiting the lowest antibacterial activity against the tested pathogens.[29] These findings indicate that organic solvents, such as ethanol and methanol, are more effective than water in extracting antibacterial compounds from this species.

An in vitro assessment of anti-inflammatory activity in LPS-stimulated RAW 264.7 macrophages revealed that treatment with *S. myrtifolium* essential oil decreased nitrite production. Remarkably, at a concentration of 25 μg/mL, nitrite levels significantly diminished by 10.18% compared with the control group. This reduction indicates that essential oils derived from the leaves exert notable inhibitory effects on inflammatory responses.[138]

Furthermore, molecular docking analysis conducted by Putri et al showed that four compounds identified from *pucuk merah* displayed lower binding energies than celecoxib. These compounds include avicularin, (S)-5,7-dihydroxy-6,8-dimethylflavanone, asamibetulinate, and ursolic acid. Explicitly, the results demonstrate that these four substances exhibit significant potential to act as COX-2 inhibitors.[136]

Syzygium myrtifolium is recognized for its high flavonoid content. Broadly, flavonoids have been reported to accelerate the wound-healing process by enhancing the upregulation of basic fibroblast growth factor in granulation tissue. These compounds also promote the synthesis of type III collagen and the expression of vascular endothelial growth factor.[139] Logically, these molecular interactions provide a strong scientific basis for the plant's traditional use. The *Syzygium myrtifolium* plant and the chemical structure of flavonoids, which are highly relevant to diabetic wound healing, are illustrated in Figure 7.

Aloe vera

Aloe vera is a prominent plant species within the Asphodelaceae family. The designation "Aloe vera" originates from the Arabic term "alloeh," meaning "shining bitter substance," and the Latin word "vera," which means "true".[140] Historically, this plant is highly esteemed in several cultural traditions for its medicinal and cosmetic applications. Since the time of ancient Egyptian civilization, *Aloe vera* has been recognized as an effective natural remedy for enhancing wound healing.[141] Globally, across regions (eg, China, Greece, Spain, India, and Iran), this species is often referred to as "the silent healer" or "the healing plant."[142]

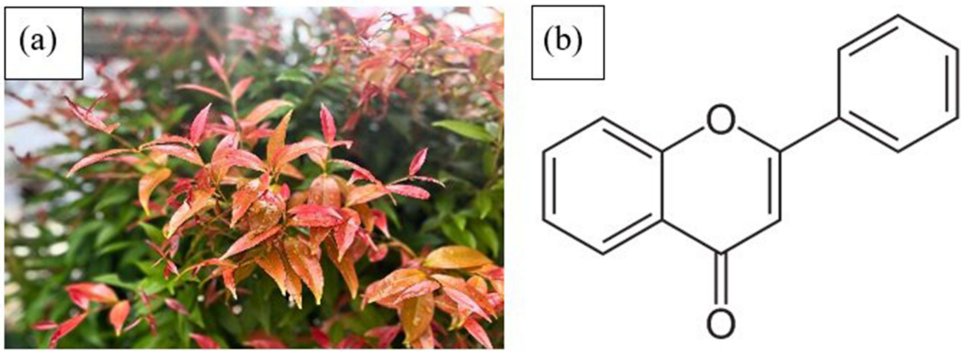

Figure 7 (**a**) *Syzygium myrtifolium* Walp. plant and (**b**) chemical structure of a flavonoid.

Clinically, *Aloe vera* exhibits a broad spectrum of pharmacological activities, including anti-inflammatory, immunomodulatory, and antibacterial effects.[143] The plant comprises a diverse assortment of bioactive constituents. These include phenolic compounds, saponins, anthraquinones,[144] glycosides, polysaccharides, pyrocatechols, acetans, phytols, oleic acid, and water-soluble polysaccharides.[145] Notably, anthraquinones found in the methanolic extract of *Aloe vera* exhibit antiglycation activity. This is achieved by inhibiting the formation of advanced glycation end products (AGEs) and N^{ε}-(carboxymethyl)lysine (CML) in a bovine serum albumin (BSA)/glucose model.[146]

The anti-inflammatory evaluation conducted by Oryan et al utilized a square excisional wound model (2 × 2 cm) across three experimental groups, namely a saline-treated control group and two treatment groups receiving *Aloe vera* at concentrations of 25 mg/mL and 50 mg/mL. Treatments were administered for 10 days, and wound progression was monitored up to day 30. Remarkably, the results exhibited a dose-dependent effect, where higher concentrations of *Aloe vera* correlated with greater wound contraction. Specifically, the injection of *Aloe vera* at a dose of 100 mg yielded the most pronounced effect. This concentration resulted in near-complete wound closure by the end of the observation period.[147]

Recent studies on the anti-inflammatory activities of *Aloe vera* have focused on the underlying molecular mechanisms of isolated aloin compounds. Specifically, research using LPS-stimulated RAW 264.7 macrophage cells provides significant insights. Aloin demonstrates potent anti-inflammatory effects by suppressing the production of pro-inflammatory cytokines and reducing ROS generation. Remarkably, it achieves this by obstructing the JAK1–STAT1/3 signaling pathway, which is essential for regulating systemic inflammatory responses.[148] The *Aloe vera* plant and the chemical structure of Aloin A, which is highly relevant to diabetic wound healing, are illustrated in Figure 8.

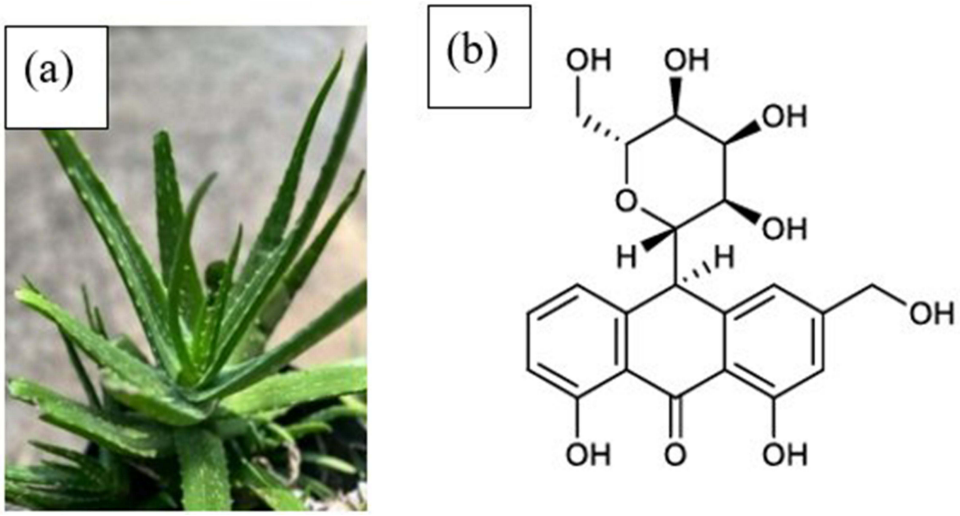

Figure 8 (**a**) *Aloe vera* plant and (**b**) chemical structure of aloin A.

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Anredera cordifolia

Anredera cordifolia is a perennial climbing plant within the Basellaceae family. In several indigenous communities across Indonesia, this plant is traditionally utilized to reduce blood glucose levels and is also frequently consumed as a leafy vegetable.[149] Distinctively, topical formulations such as ointments and gels prepared from *A. cordifolia* extracts exhibit robust antibacterial activity.[150] These preparations are commonly applied in the clinical management of burn wounds to prevent complications.[64] Phytochemical screening conducted by Dwitiyanti et al observed that the ethanolic extract of *A. cordifolia* contains several diverse classes of secondary metabolites. These include alkaloids, flavonoids, tannins, steroids, and phenolics. Quantitatively, analysis revealed that a 50 mg extract contained approximately 1.35% total flavonoids and 1.031% vitexin. Undeniably, both compounds are linked to strong antioxidant and anti-inflammatory activities.[151]

Furthermore, the results of an in vivo study conducted by Djamil et al illustrated the significant antidiabetic potential of the leaves. This was proven by a measurable decrease in blood glucose levels in diabetic animal models. Substantially, the efficacy of the extract was compared directly to that of acarbose. The experimental design utilized four distinct treatment groups. Decisively, the results showed a statistically significant reduction in blood glucose following the administration of *A. cordifolia* extract at a dose of 100 mg/kg of body weight.[152]

Consistent with these findings, topical application of a 10% *A. cordifolia* extract significantly accelerated wound closure in streptozotocin-induced diabetic rats.[153] Furthermore, recent research shows that *A. cordifolia* extract promotes wound healing in normoglycemic and hyperglycemic mice. Notably, the 10% (w/v) formulation demonstrated greater efficacy than the lower concentrations of 2.5% and 5% (w/v).[154]

The *n*-hexane fraction of *A. cordifolia* has demonstrated measurable antibacterial activity against various microorganisms, including *Staphylococcus aureus* (MIC 256 μg/mL), *Bacillus subtilis*, and *Bacillus cereus* (MIC 521 μg/mL).[155] Additionally, Nxumalo et al assessed the antimicrobial activity of *A. cordifolia* leaf extracts against *S. aureus, B. cereus, Escherichia coli*, and *Proteus mirabilis*. This assessment measured the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) while utilizing ciprofloxacin as a reference antibiotic. Ciprofloxacin showed activity against all four bacterial strains at a concentration of 25 mg/mL, with MBC values surpassing 50 mg/mL. Paradoxically, the *A. cordifolia* extract exhibited stronger antibacterial effects against *S. aureus* (MIC 0.098; MBC 25). Specifically, the extract also showed high potency against *B. cereus, E. coli* (MIC 0.391; MBC > 50), and *P. mirabilis* (MIC 0.391; MBC > 50). Inevitably, these results indicate higher efficacy of the plant extract compared with ciprofloxacin under the evaluated conditions.[156] The *A. cordifolia* plant and the chemical structure of vitexin, which is highly relevant to diabetic wound healing, are illustrated in Figure 9.

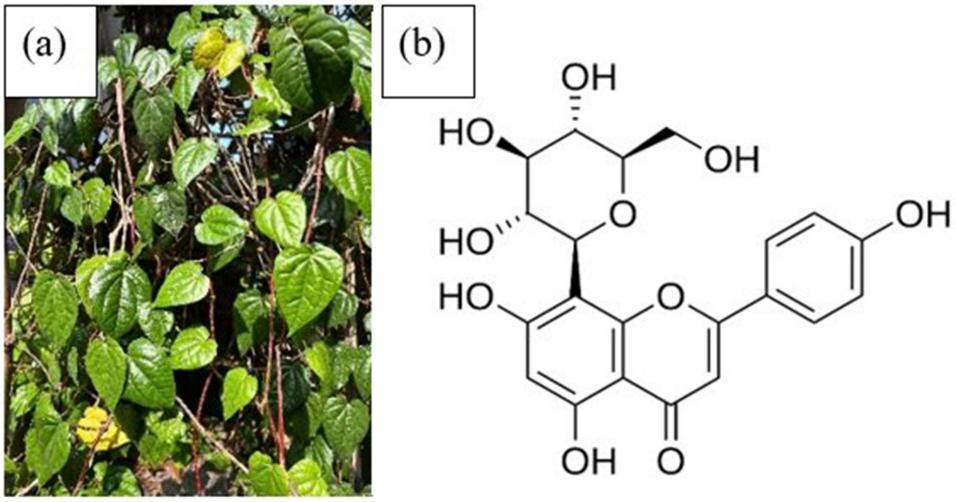

Figure 9 (**a**) *Anredera cordifolia* plant and (**b**) chemical structure of vitexin.

Ginkgo biloba

Ginkgo biloba extract is derived from the *Ginkgo biloba* tree (a member of the Ginkgoaceae family) and is widely regarded as one of the oldest living tree species in the world.[157] Historically, the Anak Dalam community has utilized *G. biloba* as a medicinal plant. They employ their seeds, leaves, and fruits for various therapeutic applications. Distinctively, these parts offer antibacterial, antioxidant, and anti-cardiovascular benefits, alongside several other pharmacological activities.[158]

The antioxidant activity of the ethanolic extract of *G. biloba* was evaluated using the DPPH radical scavenging assay and the molybdenum-reducing power (MRP) method. Among the samples, *G. biloba* originating from Košice exhibited the strongest antioxidant capacity. Remarkably, this sample showed DPPH values of 1545 ± 0.112 and MRP values of 35,485 ± 0.46.[159] Additionally, the wound-healing potential of this extract has been investigated in alloxan-induced diabetic rat models. In these studies, the extract was compared directly with a *Centella asiatica* cream formulation. Decisively, the topical formulation containing *G. biloba* extract exhibited the fastest wound closure. Full recovery was achieved by day 13 of the treatment.[160] The *G. biloba* plant and the chemical structure of ginkgolide, which is highly relevant to diabetic wound healing, are illustrated in Figure 10.

Diplazium esculentum

Diplazium esculentum is a fern species from the Athyriaceae family and is commonly found in lowland locations throughout Indonesia. Broadly, the plant is consumed by local communities as a nutritious vegetable Paradoxically, its leaves are also traditionally used as natural insect repellents, though to a lesser extent.[161] The young fronds are particularly popular as a traditional food ingredient. Customarily, these are prepared in various local dishes, including stir-fries and salads.[162]

Antioxidant evaluation of the hydroalcoholic leaf extract of *D. esculentum* (DEHAe) demonstrated notable free radical scavenging activity in vitro. Specifically, the DPPH assay indicated strong anti-inflammatory potential for this extract. Furthermore, in vivo studies utilizing streptozotocin-induced diabetic rat models showed that the administration of DEHAe at a dose of 500 mg/kg of body weight led to a reduction in fasting blood glucose levels by as much as 45.6%. Effectively, this result was nearly comparable to the effects of metformin.[162]

The methanolic extract of *D. esculentum* leaves contains numerous bioactive constituents. These include alkaloids, steroids, tannins, polyphenols, flavonoids, and saponins. Collectively, these compounds are associated with significant antibacterial activity. The antibacterial assessment, utilizing the disk diffusion method on nutrient agar, was conducted at extract concentrations of 20%, 40%, 60%, and 80%. Tetracycline served as the positive control, while dimethyl sulfoxide (DMSO) was used as the negative control. Remarkably, the results exhibited quantifiable inhibitory effects against common pathogens. The average inhibition zones reached 5.90 mm for *Pseudomonas aeruginosa* and 5.69 mm for *Staphylococcus epidermidis*.[163] The *D. esculentum* plant and the chemical structure of saponin, which is highly relevant to diabetic wound healing, are illustrated in Figure 11.

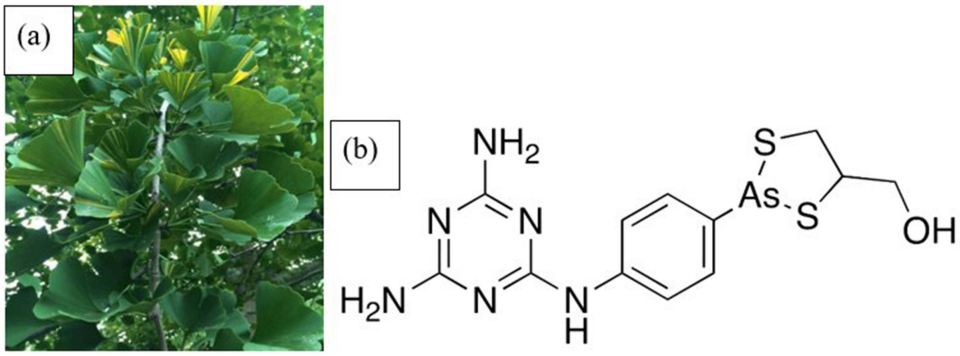

Figure 10 (**a**) *Ginkgo biloba* plant[49] and (**b**) chemical structure of ginkgolida.

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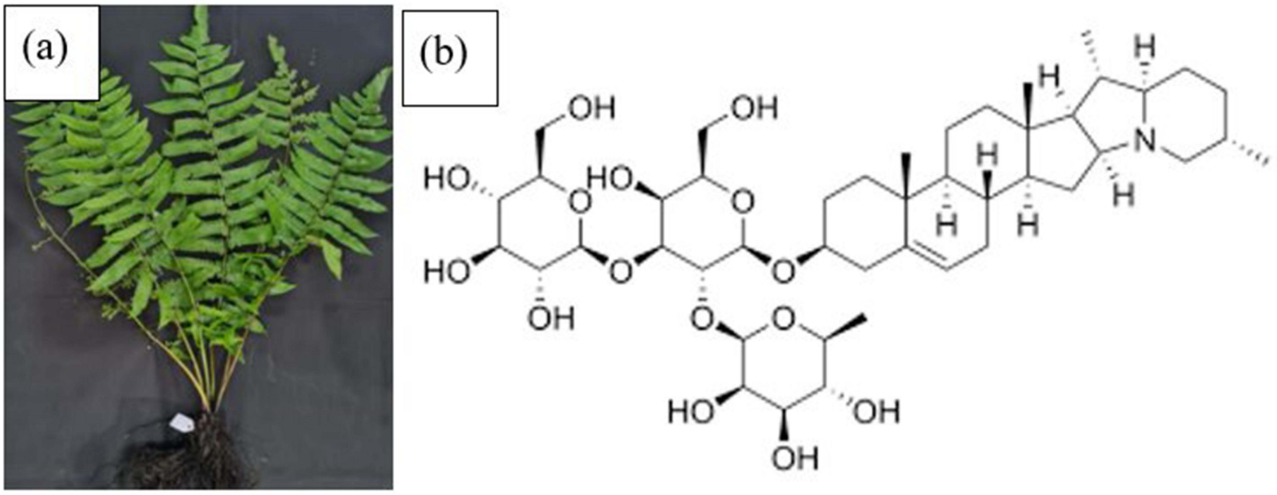

Figure 11 (**a**) *Diplazium esculentum* plant[54] and (**b**) chemical structure of saponin.

Goniothalamus macrophyllus

Goniothalamus macrophyllus is a distinct plant species within the genus *Goniothalamus*, belonging to the Annonaceae family. It features medium-sized, aromatic stems and elongated leaves that typically measure 40 to 55 cm in length and 7 to 15 cm in width. Uniquely, these leaves possess tapered apices and a characteristic fragrance.[164] Across Indonesia, particularly in Kalimantan and Java, various plant parts, including the leaves, roots, and bark, are empirically utilized as decoctions. Traditionally, these preparations treat fever, headaches, and rheumatic diseases, while also serving as a component of postpartum therapy.[72] Notably, the Anak Dalam tribe uses this plant for wound care by pounding the bark. Specifically, the liquid is squeezed out and applied directly to the affected area.[26]

The wound-healing potential of *G. macrophyllus* in diabetic conditions is closely linked to its anti-inflammatory activity. Research conducted by Teruna et al indicated that (2S)-pinocembrin (a compound isolated from this plant) markedly suppressed LPS-induced prostaglandin E_2 (PGE_2) production in vitro. Using RAW 264.7 and U937 macrophage cell lines, the study recorded IC_{50} values of 75.9 μM and 86.4 μM, respectively. Correspondingly, these findings were corroborated by molecular interaction analyses. These tests showed that (2S)-pinocembrin demonstrates a robust binding affinity toward p38α and ERK2 proteins within the MAPK signaling pathway. Substantially, this pathway is responsible for regulating COX-2 expression. Decisively, these results suggest that (2S)-pinocembrin has considerable potential as an anti-inflammatory candidate. This compound effectively mitigates the excessive inflammatory responses that often impair the natural healing process in diabetic patients.[165] The *G. macrophyllus* plant and the chemical structure of pinocembrin, which is highly relevant to diabetic wound recovery, are illustrated in Figure 12.

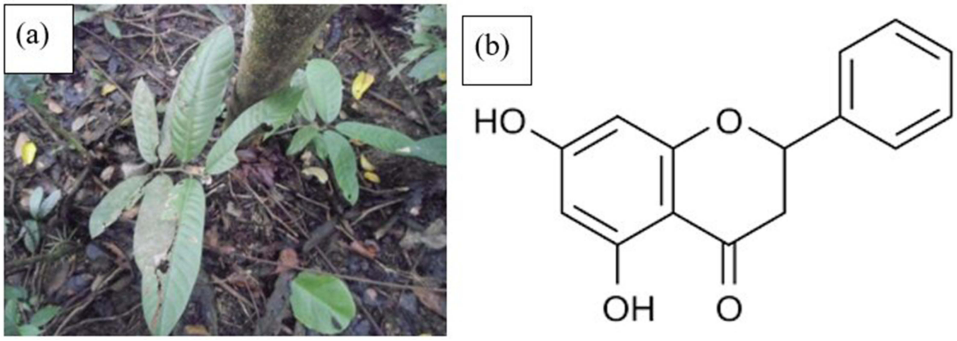

Figure 12 (**a**) *Goniothalamus macrophyllus* plant[57] And (**b**) chemical structure of pinocembrin.

Persea americana

The avocado (*Persea americana*), a prominent member of the Lauraceae family, represents a versatile botanical resource where nearly every part is traditionally utilized. Scientifically, these components are recognized for a wide range of pharmacological activities, including antioxidant, anti-inflammatory, analgesic, and antimicrobial effects. Furthermore, research supports its role in antidiabetic, antihypertensive, and hepatoprotective applications, alongside properties that significantly enhance wound healing and skin care.[166]

A study conducted by Rosa et al demonstrated that leaf extracts of *P. americana* exhibit wound-healing activity comparable to povidone-iodine, particularly at concentrations of 10% to 15%. Interestingly, this impact is linked to molecular mechanisms that inhibit nuclear factor kappa B1 (NF-*κ*B1), which is a crucial regulator of inflammatory responses and tissue remodeling. Utilizing a methodology that incorporated in vivo experiments and molecular docking, the researchers identified quercetin, catechin, and epicatechin as major active constituents. Persuasively, these compounds work together to accelerate wound closure, attenuate inflammation, and promote tissue regeneration.[167]

Research by Ekom et al indicates that the methanolic extract of *P. americana* seeds possesses significant antibacterial activity and promotes healing in animal models with *Staphylococcus aureus*-infected wounds. Substantially, the observed effects were ascribed to multiple mechanisms, including the breakdown of bacterial membrane integrity and the leakage of cytoplasmic contents. Furthermore, these compounds work by blocking the H^+-ATPase proton pump and suppressing biofilm formation. Resultantly, topical gel formulations containing the extract demonstrated enhanced wound closure and a significant reduction in bacterial colony counts. These preparations were also verified as safe, with no instances of skin or ocular irritation. Collectively, the findings underscore the potential of *P. americana* seed extract as a natural therapeutic agent for managing skin infections.[50]

Consistent with these findings, Etefa et al assessed the antibacterial activity of *P. americana* peel extract. Notably, the study reported significant inhibition zones against *Bacillus cereus, Salmonella typhi*, and *Staphylococcus aureus*, measuring 20 ± 1.2 mm, 19 ± 0.2 mm, and 18 ± 0.5 mm, respectively. Logically, the substantial antibacterial activity observed suggests that *P. americana*-derived extracts serve as promising candidates for supporting wound-healing applications.[168] The *Persea americana* plant and the chemical structure of epicatechin, which is highly relevant to diabetic wound healing, are illustrated in Figure 13.

Carica papaya

Carica papaya (a member of the Caricaceae family) is a large herbaceous plant widely distributed across more than 50 tropical and subtropical regions worldwide. Traditionally, various parts of the plant (eg, the leaves, seeds, latex, and both ripe and unripe fruits) are consumed as food and utilized in medicinal practices.[169] Scientifically, extensive pharmacological studies demonstrate that this species possesses a broad spectrum of bioactivities. These include antioxidant,

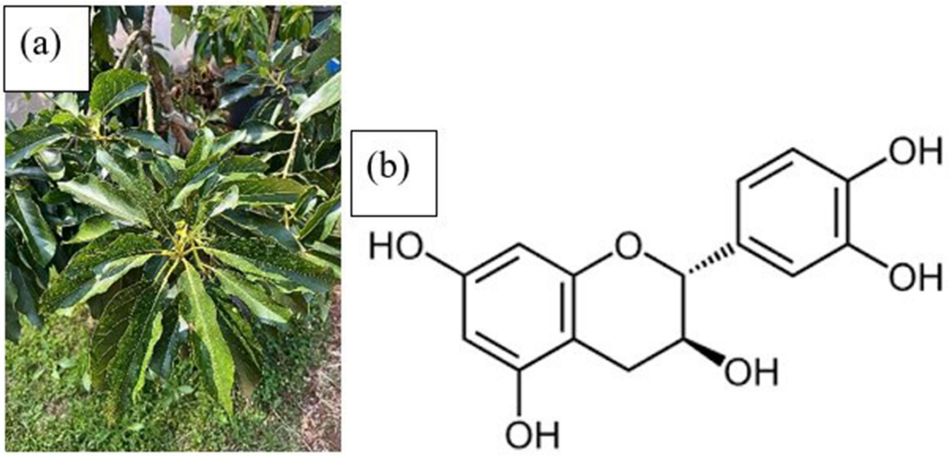

Figure 13 (**a**) *Persea americana* plant and (**b**) chemical structure of epicatechin.

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antihypertensive, and wound-healing properties. Furthermore, the plant exhibits hepatoprotective, anti-inflammatory, antimicrobial, antifungal, antifertility, histaminergic, diuretic, anti-amoebic, antitumor, anthelmintic, smooth muscle–modulating, antimalarial, hypoglycemic, immunomodulatory, anti-ulcer, and anti-sickling effects.[170]

Research conducted by Li et al further demonstrated that methanolic and aqueous extracts derived from green and yellow papaya exhibit significant antidiabetic and wound-healing activities. Remarkably, yellow papaya seeds were found to contain the highest levels of polyphenols and flavonoids. These seeds displayed antioxidant activity approximately five to ten times greater than that of green papaya. Conversely, extracts from green papaya pulp consistently augmented glucose absorption. Effectively, this process elevated the expression of glucose transporter 2 (GLUT2) in hepatic cells and glucose transporter 4 (GLUT4) in muscle cells. Moreover, seed extracts from both papaya varieties markedly promoted fibroblast migration and collagen synthesis by up to two- to threefold. Substantially, these actions highlight the plant's potential for diabetes management and the therapy of associated wound complications.[171]

C. papaya leaf extract contains high concentrations of secondary metabolites, including saponins, flavonoids, alkaloids, and phenolic compounds. Broadly, these constituents contribute to its notable antioxidant activity, measured at an IC_{50} of 0.236 mg/mL. The extract also increases fibroblast proliferation by up to 85% and enhances cell migration by 78.7% within 48 hours. Concurrently, it stimulates collagen synthesis, suggesting a potent role in natural wound-healing processes.[172] Moreover, *C. papaya* has been documented to inhibit aldose reductase and sorbitol dehydrogenase. Correctly, these are essential enzymes involved in the polyol pathway, meaning the plant contributes to the attenuation of diabetic complications through antiglycative effects.[173]

Saponins represent a particularly significant bioactive component of *C. papaya* in the context of tissue repair. These compounds demonstrate the ability to enhance regeneration and reduce scar formation by increasing nitric oxide (NO) production. Appropriately, this process improves blood flow to the affected area. Saponins also suppress the excessive fibroblast proliferation often linked to fibrosis and downregulate the expression of α-smooth muscle actin (α-SMA). Precisely, through these molecular mechanisms, saponins inhibit the development of fibroblasts into myofibroblasts. Substantially, this inhibition is a key factor in preventing the formation of dense scar tissue.[174] The *C. papaya* plant and the chemical structure of saponin, which is highly relevant to diabetic wound healing, are illustrated in Figure 14.

Momordica charantia L

Momordica charantia L. is a distinct plant species within the Cucurbitaceae family. This family comprises approximately 47 species distributed across Africa and 12 species found in Asia and Australia.[175] Traditionally, the plant is renowned

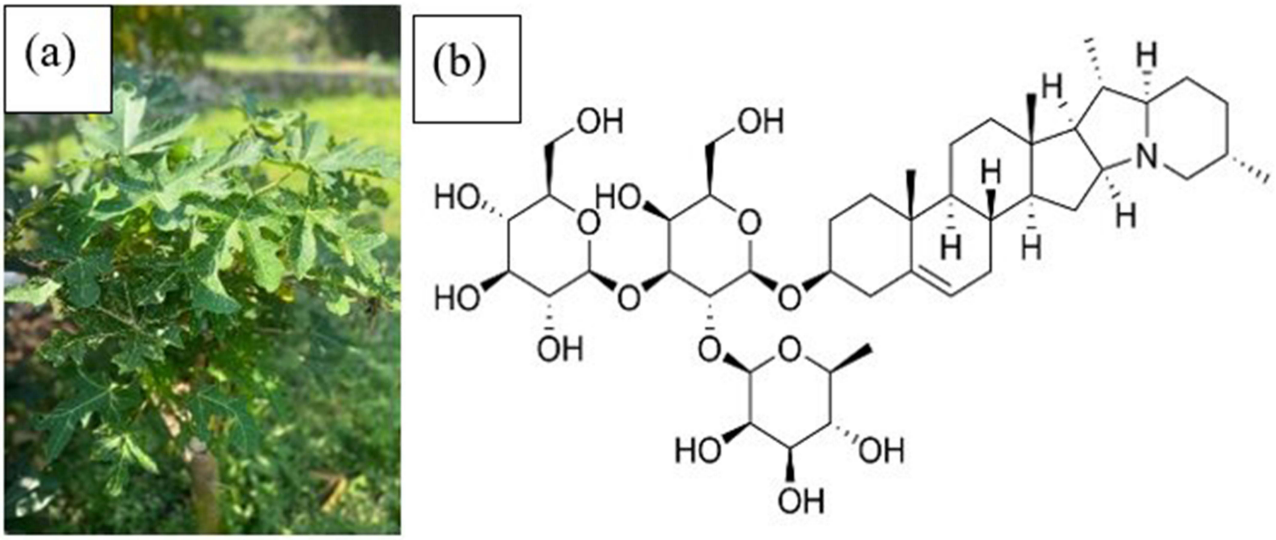

Figure 14 (**a**) *Carica papaya* plant and (**b**) chemical structure of saponin.

for its characteristic bitter flavor. Sensibly, this bitterness is ascribed to the presence of specific compounds such as 3-O-malonylmomordicine I, momordicine I, and (23E)-3β-O-malonyl-7β,25-dihydroxycucurbita-5,23-dien-19-al. [176]

M. charantia possesses a plethora of bioactive constituents, including charantin, insulin-like polypeptides, lectins, and cucurbitanoids. Inevitably, these elements work alongside saponins, flavonoids, and alkaloids to support diverse pharmacological properties. These activities encompass antidiabetic, antioxidant, antitumor, anti-inflammatory effects, and hypolipidemic effects.[177] Among its phytochemical components, triterpenoids (eg, momordisin, charantin, cuguacin, and caravilagenin) have been identified as major constituents.[178]

A study by Sagástegui-Guarniz et al indicated that a 1% topical gel and cream of *M. charantia* leaf extract significantly accelerated the wound-healing process in mouse skin models. Remarkably, the cream formulation exhibited the greatest efficacy. This success was evidenced by significant improvements in wound closure and tissue regeneration. Specifically, the treatment improved fibroblast migration, increased collagen deposition, and ensured optimal re-epithelialization. Substantially, these therapeutic effects are believed to be facilitated by bioactive compounds in the leaves. These include flavonoids, steroids, and cucurbitane-type triterpenoids, which exhibit strong antioxidant and antimicrobial properties. Furthermore, these compounds inhibit NF-κB signaling while upregulating the expression of transforming growth factor-beta (TGF-β).[179]

A systematic review and meta-analysis of 10 clinical trials, involving 1,045 participants, demonstrated that *M. charantia* extract has the potential to significantly reduce fasting plasma glucose (FPG), postprandial glucose (PPG), and glycated hemoglobin levels (HbA1c) compared with a placebo. Importantly, these results occurred without the onset of serious adverse effects.[180] The *M. charantia* plant and the chemical structure of momordisin, which is highly relevant to diabetic wound healing, are illustrated in Figure 15.

Centella asiatica

Centella asiatica is a perennial herbaceous plant classified within the Apiaceae family (Umbelliferae). It holds considerable traditional relevance, especially in Southeast Asia, where the species is esteemed for its nutritional qualities.[181] Historically, this plant has been extensively utilized in numerous therapeutic applications. These include its antimicrobial, antioxidant, anti-inflammatory, and neuroprotective effects. Unquestionably, its ability to promote wound healing remains its most well-established clinical application.[182]

The therapeutic effects of *C. asiatica* are mainly attributed to four principal pentacyclic triterpenoids, namely asiaticoside, madecassoside, asiatic acid, and madecassic acid. Effectively, these substances exhibit distinct pharmacological characteristics despite possessing analogous core structures. The glycosidic forms (ie, asiaticoside and madecassoside) are typically more prevalent and demonstrate greater solubility compared to their aglycone counterparts. Appropriately, these molecules display pronounced anti-inflammatory, antioxidant, and immunomodulatory

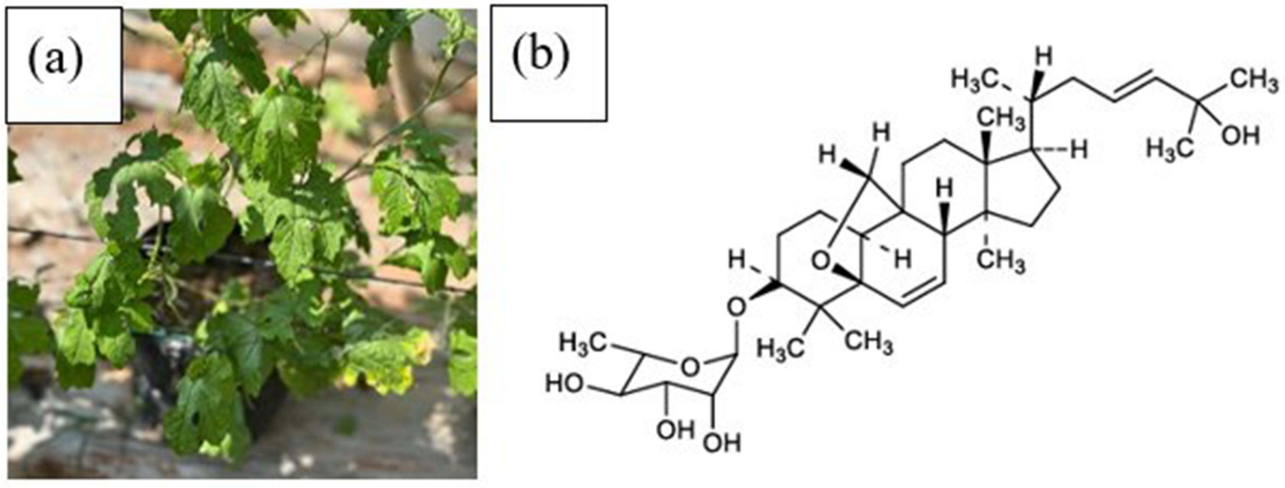

Figure 15 (**a**) *Momordica charantia* L plant and (**b**) chemical structure of momordisin.

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activities.[183] Asiaticoside and madecassoside have been shown to enhance collagen synthesis and promote skin tissue regeneration. Conversely, asiatic acid and madecassic acid facilitate wound repair by stimulating fibroblast activity. Furthermore, these acids work by suppressing pro-inflammatory mediators, such as tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6).[184]

A study by Xiao et al demonstrated that *C. asiatica* accelerates diabetic wound healing chiefly through anti-inflammatory mechanisms involving the AKT/MAPK/NF-κB signaling pathway. In an in vitro model using RAW264.7 macrophages stimulated with advanced glycation end products (AGEs), treatment with the extract significantly reduced NO production and downregulated iNOS expression. Remarkably, the application also suppressed the release of proinflammatory cytokines, including IL-6, IL-16, and TNF-α. Western blot and qRT-PCR analyses further corroborated these results. Specifically, these tests confirmed the inhibition of NF-κB phosphorylation and a measurable reduction in AKT/MAPK pathway activation. Consistent with the in vitro findings, in vivo experiments on diabetic mice revealed that topical application of *C. asiatica* at a dose of 200 $\mu g/cm^2$ significantly improved wound closure. Substantially, the treated subjects showed increased collagen deposition and promoted re-epithelialization compared with the control group.[185] Consequently, these results support the potential use of *C. asiatica* as a supplementary therapeutic agent in the treatment of diabetic wounds. The *C. asiatica* plant and the chemical structure of asiaticoside, which is highly relevant to diabetic wound healing, are illustrated in Figure 16.

Moringa oleifera

Moringa oleifera, commonly known as the moringa tree, is recognized as a prolific and economical source of phytochemicals. Consequently, it is frequently utilized by the Anak Dalam community for its broad medicinal potential.[186] For centuries, this plant has been used in traditional medicine to manage a variety of conditions, such as malnutrition, diabetes, and anemia. Historically, it has also addressed hypertension, stress-related disorders, skin diseases, and kidney stones. Broadly, these benefits are attributed to its potent antioxidant, anti-inflammatory, and anticancer properties.

Muthumanickam and Palanivel successfully isolated the flavonoid gossypetin from *M. oleifera* leaves to evaluate its biological activities. The compound was initially identified by thin-layer chromatography (TLC) and further characterized by GC–MS, UV–Vis spectroscopy, FTIR, XRD, and thermogravimetric analysis (TGA). Appropriately, the results indicated that gossypetin demonstrates significant antioxidant activity (IC_{50} = 75 μg/mL). Distinctively, the compound also shows notable antibacterial properties against *Escherichia coli, Pseudomonas aeruginosa, Klebsiella pneumoniae, and Enterococcus faecalis*. Furthermore, it possesses the capacity to prevent the formation of harmful biofilms.[187] Gossypetin has been shown to suppress the proliferation and migration of vascular smooth muscle cells (VSMCs). Remarkably, this modulates post-injury vascular remodeling by downregulating NF-κB and protein kinase B (PKB/Akt) signaling pathways. Additionally, it reduces the expression and activity of matrix metalloproteinase-9 (MMP-9).

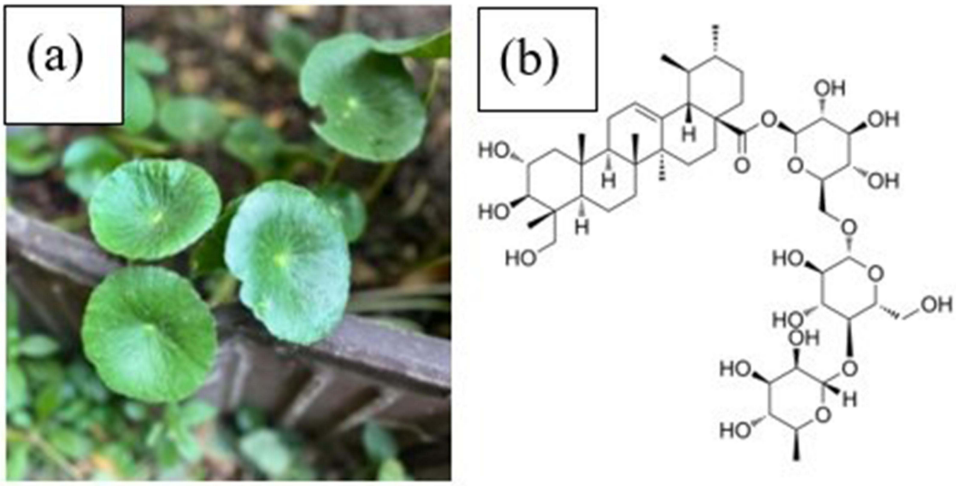

Figure 16 (**a**) *Centella asiatica* plant and (**b**) chemical structure of asiaticoside.

Substantially, these mechanisms collectively support improved wound-healing processes. Decisively, the plant promotes controlled inflammatory responses while simultaneously enhancing tissue repair.[188]

A study reported that the aqueous fraction of *Moringa oleifera* leaves demonstrates potent antibacterial properties and enhances recovery in diabetic rat models. Effectively, this fraction suppresses the proliferation of *Staphylococcus aureus, Pseudomonas aeruginosa*, and *Escherichia coli*. Using a minimum inhibitory concentration (MIC) of 3,125 μg/mL, the extract showed a clear ability to control bacterial growth. In a diabetic wound model, the topical application of the aqueous fraction at concentrations of 0.5%, 1%, and 2% led to expedited wound contraction over a 21-day period. Remarkably, the treatment also improved tissue regeneration and caused a significant decrease in inflammatory mediators. These include TNF-α, IL-1β, IL-6, iNOS, and COX-2. Substantially, the therapeutic effects are believed to be principally linked to the bioactive compound vicenin-2 found within the aqueous fraction.[189] The *Moringa oleifera* plant and the chemical structure of gossypetin, which is highly relevant to diabetic wound healing, are illustrated in Figure 17.

Psidium guajava

Psidium guajava (a member of the Myrtaceae family) or guava is extensively utilized as a nutritional food source and a traditional medicine. Locally, it is relied upon for the management of several ailments, such as diabetes, hypertension, and fever.[190] Scientifically, numerous studies have corroborated its effectiveness in treating wounds and pain. Specifically, wound-healing activity evaluated in diabetic mouse models revealed that a 10% gel formulation containing the leaf fraction exhibited the most significant healing effect. Unquestionably, this concentration outperformed the diabetic control group and the 5% gel alternative.[191]

Guava leaves are abundant in various antioxidant compounds, encompassing polyphenols like gallic acid, caffeic acid, ferulic acid, chlorogenic acid, and ellagic acid. Additionally, these leaves contain essential flavonoids such as kaempferol, quercetin, myricetin, catechins, epicatechins, and rutin. Appropriately, the presence of terpenoids (eg, limonene and β-caryophyllene), anthocyanins (cyanidin-3-O-glucoside), tannins (ellagic acid and procyanidin B2), and vitamin C further enriches the plant's chemical profile. Collectively, these compounds contribute to the broad pharmacological capabilities of the plant. Remarkably, they work together to provide strong antioxidant, anti-inflammatory, and anticarcinogenic activities.[192]

Furthermore, quercetin-3-O-sulfate was identified as the principal phenolic compound in the ethanolic extract of the leaves. Distinctively, this specific molecule demonstrates greater antioxidant activity than standard quercetin. Substantially, it also exhibits significant antidiabetic and anticoagulant properties.[193] The guava plant and the chemical structure of quercetin-3-O-sulfate, which is highly relevant to diabetic wound recovery, are illustrated in Figure 18.

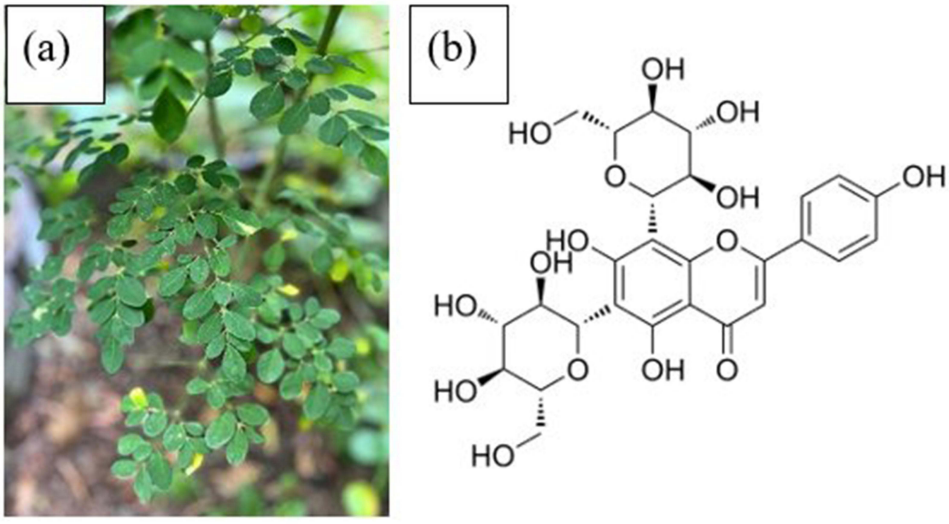

Figure 17 (**a**) *Moringa oleifera* plant and (**b**) chemical structure of gossypetin.

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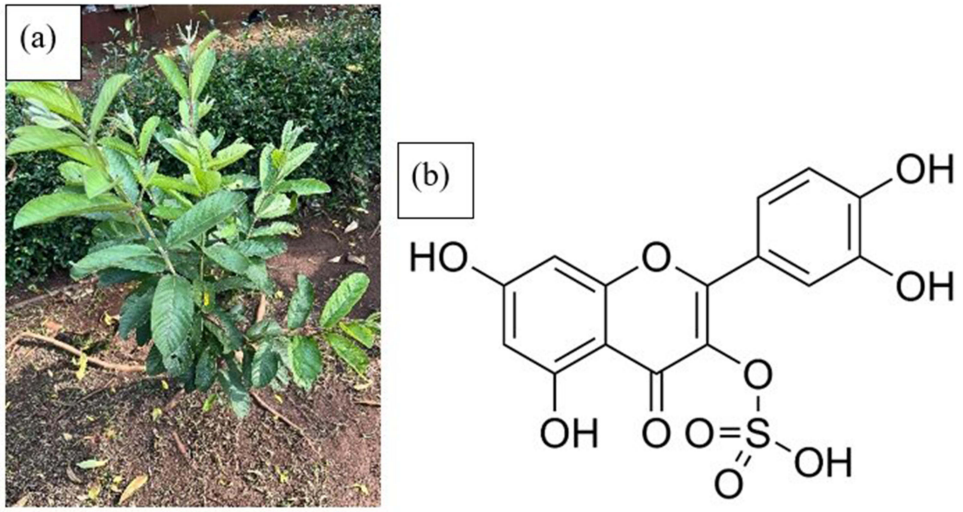

Figure 18 (**a**) *Psidium guajava* plant and (**b**) chemical structure of quercetin-3-O-sulfate compound.

Overall, several medicinal plants reviewed in this study demonstrate antioxidant, anti-inflammatory, and antibacterial activities relevant to wound healing. Interestingly, the strength and consistency of evidence vary considerably among species. Plants such as *Anredera cordifolia* and *Centella asiatica* are supported by relatively abundant in vivo studies. Specifically, these investigations demonstrate enhanced wound contraction, collagen deposition, and re-epithelialization. Conversely, other plants are primarily supported by in vitro assays evaluating antioxidant or antimicrobial activity. Regarding antioxidant activity, flavonoid-rich plants, including *Psidium guajava* and *Syzygium* species, consistently show a strong free radical scavenging capacity. Appropriately, anti-inflammatory effects are frequently associated with compounds such as quercetin, catechins, and triterpenoids. These molecules work by modulating key signaling pathways, including NF-κB and MAPK. Furthermore, antibacterial activity, particularly against *Staphylococcus aureus* and *Pseudomonas aeruginosa*, is commonly reported. Logically, these results vary depending on the extract type and the experimental model used. Substantially, these findings indicate that while many plants exhibit multiple bioactivities, the level of supporting evidence and relative efficacy differ across studies.

Current Status of Research and Challenges

Research regarding the utilization of medicinal plants by the Anak Dalam tribe for treating diabetic wounds remains in the early stages of scientific development. Predominantly, existing studies focus on phytochemical characterization and preliminary evaluations of biological activity. Notably, there is a limited geographic representation in current literature, particularly concerning the Indonesian context. Substantially, this gap highlights the need for systematic documentation and broader data collection to understand the therapeutic potential of these plants fully.

A major challenge in this field lies in the systematic collection and accurate taxonomic identification of plant species. Explicitly, these tasks are difficult in the remote forest environments where the Anak Dalam community resides. Ethical considerations are also essential since research involving indigenous knowledge requires culturally sensitive approaches and fair benefit-sharing mechanisms. Appropriately, another critical challenge involves the integration of orally transmitted ethnomedical knowledge into scientific frameworks. Traditional practices are often described qualitatively. Logically, this makes it difficult to standardize variables such as dosage and preparation methods, thereby complicating their correlation with measurable pharmacological outcomes.

Currently, most evidence is derived from in vitro assays and in vivo studies using experimental animal models. However, well-designed clinical trials involving human subjects remain scarce. Furthermore, limited data on toxicity, pharmacokinetics, and the bioavailability of active compounds present significant barriers to evaluating long-term safety. Inevitably, variability in extraction methods and dosing protocols contributes to inconsistencies in reported findings.

Future Perspectives

To strengthen the scientific foundation and enhance the credibility of future research, standardized and rigorous study designs are necessary. These designs must include comprehensive toxicological assessments, pharmacodynamic evaluations, and controlled clinical trials. Collaborative, multidisciplinary approaches involving researchers, healthcare professionals, and the Anak Dalam community remain essential. Substantially, such partnerships ensure scientific validity and ethical integrity throughout the discovery process.

Future research should also prioritize the integration of traditional knowledge with modern analytical techniques. Explicitly, the use of phytochemical profiling and molecular mechanism studies helps to better elucidate the bioactive compounds involved in tissue repair. Furthermore, long-term and context-specific studies are required to support the translation of these medicinal plants into clinical practice. These efforts will pave the way for safe, effective, and sustainable therapeutic strategies for diabetic wound management.

Conclusions

Medicinal plants traditionally used by the Anak Dalam tribe in Jambi Province, including *Syzygium myrtifolium* Walp., *Centella asiatica, Curcuma longa*, and *Zingiber cassumunar*, represent valuable candidate sources for diabetic wound-healing research. These plants contain diverse bioactive phytochemicals such as flavonoids, phenolic compounds, terpenoids, and saponins. Importantly, these constituents are associated with antioxidant, anti-inflammatory, and antibacterial activities. Evidence from in vitro and in vivo pharmacological studies suggests that these bioactive compounds support essential biological processes, including re-epithelialization and angiogenesis. Remarkably, the application of these extracts also promotes significant collagen deposition within the wound site.

Nevertheless, the current evidence remains largely preclinical and heterogeneous. Validation in well-designed clinical studies is currently limited. Consequently, this review does not establish clinical efficacy for diabetic ulcer treatment or a direct causal relationship with wound healing specifically within the tribe's traditional context. Further research is required to identify specific active constituents and evaluate long-term safety. Substantially, the standardization of extract formulations is a prerequisite before these plants can be advanced toward phytopharmaceutical or topical therapeutic applications.

Overall, this review provides a candidate-generating scientific synthesis of medicinal plants used in traditional knowledge. Effectively, it highlights the need for ethically conducted and scientifically rigorous studies. Such research must integrate indigenous wisdom with modern pharmacological validation.

Abbreviations

AP-1, activator protein-1; COX-2, cyclooxygenase-2; eNOS, endothelial nitric oxide synthase; GIP, glucose-dependent insulinotropic polypeptide; GLP-1, glucagon-like peptide-1; GLUT2, glucose transporter 2; GPx, glutathione peroxidase; GST, glutathione S-transferase; HOMA-β, homeostatic model assessment of β-cell function; HOMA-IR, homeostatic model assessment of insulin resistance; IL, interleukin; iNOS, inducible nitric oxide synthase; MAPK, mitogen-activated protein kinase; NF-κB, nuclear factor kappa B; NO, nitric oxide; Nrf2, nuclear factor erythroid 2-related factor 2; ROS, reactive oxygen species; SGLT1, sodium-glucose cotransporter 1; SOD, superoxide dismutase; TNF-α, tumor necrosis factor-alpha.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare no potential conflicts of interest regarding the research, authorship, or publication of this manuscript.

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