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POLYHERBAL WOUND HEALING FORMULATIONS INCORPORATING AEGLE MARMELOS AND CALOTROPIS PROCERA: AN EVIDENCE-BASED REVIEW

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ABSTRACT

Maintaining the continuity and protective function of skin is vital to overall human health, and any breach in this continuity demands an efficient reparative response. Traditional plant-derived medicines have gained renewed scientific interest as potential wound healing agents because of their multifaceted pharmacological properties, relative safety, and accessibility. The present review explores the therapeutic utility of two well-documented medicinal plants — Aegle marmelos (Bael) and Calotropis procera (Madar) — in the context of polyherbal wound healing formulation development. Both plants have been extensively used in Ayurvedic, Siddha, and Unani systems of medicine and carry a rich legacy of application in skin-related disorders. This article provides a systematic account of wound classification schemes, the sequential biological events underlying tissue repair, the botanical and pharmacognostic profiles of the two selected species, the phytochemical basis of their wound healing activity, and the emerging role of modern localized drug delivery systems in optimizing therapeutic outcomes. The significance of key endogenous growth factors in mediating the repair cascade is also addressed. Collectively, the available scientific data suggest that a synergistic polyherbal combination of these two botanicals holds considerable promise for the development of safe, effective, and affordable wound care formulations, warranting formal preclinical and clinical validation.

KEYWORDS: Aegle marmelos, Calotropis procera, wound healing, polyherbal formulation, drug delivery systems, phytochemicals, tissue regeneration, Ayurveda.

1. INTRODUCTION

Human skin, the largest organ of the body, functions as the primary physical and immunological barrier between the internal milieu and the external environment. Any event that disrupts the structural continuity of this barrier — be it mechanical, thermal, chemical, microbiological, or immunological in origin — gives rise to a wound.[1] Wound formation triggers an elaborate cascade of molecular and cellular events collectively aimed at restoring tissue architecture and barrier function. Failure of this process, or its prolongation beyond acceptable limits, leads to chronic non-healing wounds that impose a considerable burden on patients and healthcare systems alike.[2,3]

The physiological classification of wounds broadly distinguishes between acute and chronic forms. Acute wounds, such as those resulting from surgical procedures or minor accidental trauma, resolve within a predictable timeframe through the coordinated activity of platelets, immune cells, fibroblasts, and keratinocytes.[4,5] Chronic wounds, by contrast, become trapped in a pathological cycle of persistent inflammation, excessive protease activity, and deficient angiogenesis, preventing the orderly progression through healing stages. Diabetic foot ulcers, pressure injuries, and venous leg ulcers are well-recognized examples of this clinically challenging category.[6,7]

The biology of wound repair is governed by an orchestrated sequence of overlapping events: an initial haemostatic response, a phase of inflammatory recruitment, a period of cellular proliferation and new tissue deposition, and finally a remodelling phase that determines the long-term quality and strength of the repaired tissue.[8,9] Each of these events is regulated by a network of growth factors, cytokines, extracellular matrix components, and their respective receptor systems.

Historically, botanical preparations have played a central role in wound management across virtually all traditional medical systems. Their therapeutic attributes derive from chemically diverse secondary metabolites — including phenolics, flavonoids, alkaloids, tannins, terpenoids, and essential oils — that exert complementary biological actions encompassing antimicrobial, antioxidant, anti-inflammatory, and pro-regenerative effects.[10] Among the large number of plants documented in Ayurvedic wound care literature, Aegle marmelos and Calotropis procera have consistently featured as important remedies for skin injuries, burns, ulcers, and infections.[11]

This review aims to present a consolidated, evidence-based account of the wound healing potential of these two botanicals, with attention to their phytochemical underpinnings, mechanisms of therapeutic action, and applicability within modern advanced drug delivery frameworks.

2. WOUND: DEFINITION AND CLASSIFICATION

2.1 Definition

In the simplest sense, a wound represents a disruption of the normal structural and functional continuity of biological tissue, which may be restricted to the surface epithelium or may extend into deeper anatomical layers.[11,12] The causative agent may be external — such as a mechanical force or corrosive chemical — or internal, as in the case of ischaemic or immunologically mediated tissue damage.

2.2 Classification

Wounds are categorized along multiple axes depending on the clinical context:

A) According to Mechanism of Injury

Blunt force applied to soft tissue can produce abrasions at the skin surface, deeper contusions (bruises), or lacerations when the tissue is torn rather than cleanly cut. Sharp instruments produce incised wounds or, if the penetrating object is narrow, stab and puncture injuries. High-velocity projectiles from firearms cause unique injury patterns combining penetrating trauma with shock-wave tissue disruption.[13]

B) According to Environmental Exposure

In open wounds, the damaged tissue is directly exposed to the external environment, increasing the risk of contamination and infection. Closed wounds, such as haematomas and crush injuries, confine damaged tissue beneath an intact skin surface, limiting external contamination but predisposing to compartment syndrome and internal haemorrhage.[13]

C) According to Tissue Depth

Partial-thickness wounds involve damage confined to the epidermis and superficial aspects of the dermis, whereas full-thickness wounds extend through all dermal layers and may involve subcutaneous fat, fascia, muscle, or bone, requiring more complex and prolonged management.[13]

D) According to Healing Trajectory

Wounds that proceed through the expected sequence of repair within a normal timeframe are termed acute. Those that stall in the inflammatory phase and fail to achieve healing within three months despite appropriate treatment are classified as chronic wounds and typically require specialized wound care interventions.[14]

E) According to Infection Risk

Surgical wound classification recognizes four grades of contamination risk: Class I (clean) wounds are uninfected operative wounds with no breach of the respiratory, alimentary, or genitourinary tracts; Class II (clean-contaminated) involves controlled entry into these tracts; Class III (contaminated) includes open traumatic wounds or major breaches of sterile technique; and Class IV (dirty/infected) wounds contain devitalized tissue or established infection prior to surgery.[13]

3. PHASES OF WOUND HEALING

Tissue repair is a dynamic and precisely regulated biological phenomenon in which cellular components and biochemical mediators collaborate to replace lost or damaged tissue and restore structural integrity. The repair process is conventionally described in four partially overlapping phases:[8,9]

3.1 Haemostasis

Within seconds to minutes of vascular injury, a sequence of protective haemostatic events is initiated to minimize blood loss. Injured vessels constrict reflexively, and circulating platelets adhere to the exposed subendothelial collagen, becoming activated in the process. Activated platelets aggregate and release vasoconstrictive substances as well as mitogenic mediators including platelet-derived growth factor (PDGF), which recruits fibroblasts and smooth muscle cells to the wound. The intrinsic coagulation cascade is simultaneously triggered, converting fibrinogen to fibrin and forming a stable clot that physically seals the breach and provides a temporary matrix for cellular infiltration. Upon drying, this clot forms a protective eschar that shields the wound during subsequent repair stages.[19]

3.2 Inflammation

Overlapping with haemostasis and persisting for up to 24 hours, the inflammatory phase recruits immune effector

cells to the wound microenvironment. Vasoactive mediators, notably histamine and serotonin released from mast cells and platelets, increase local vascular permeability and promote the exudation of plasma proteins. Neutrophils are the first leucocytes to arrive, clearing bacteria and cellular debris through phagocytosis. Monocytes subsequently differentiate into macrophages that further cleanse the wound and secrete a range of pro-healing cytokines, preparing a suitable biological substrate for tissue reconstruction.[20]

3.3 Proliferation and Granulation Tissue Formation

Beginning around day four and continuing until approximately day 21, this phase is characterized by the active reconstruction of the damaged tissue compartment. Fibroblasts and epithelial cells migrate into the wound, driven by chemotactic gradients established by macrophage-derived mediators. Fibroblasts synthesize large quantities of collagen that impart mechanical strength to the forming granulation tissue. Capillary sprouting (angiogenesis) re-establishes the microvascular supply, while lymphatic vessels re-enter the tissue to restore fluid drainage. Progressive wound contraction, mediated by specialized myofibroblasts, reduces the area requiring epithelialization.

3.4 Remodelling and Scar Maturation

The final phase, which may span several months to over a year, involves the progressive reorganization of the immature collagen network laid down during the proliferative phase. Type III collagen is gradually replaced by the mechanically superior type I collagen, and collagen fibres are reoriented along tension lines to maximize tensile strength. The ultimate physical properties and cosmetic appearance of the scar are determined during this remodelling phase, and dysregulation at this stage can result in hypertrophic or keloid scar formation.[21]

4. MEDICINAL PLANTS IN AYURVEDIC WOUND HEALING

4.1 Calotropis procera (Ait.) R.Br. — Madar / Aak

Calotropis procera is a perennial xerophytic shrub or small laticiferous tree belonging to the family Apocynaceae. Widely distributed across the arid and semi-arid zones of South and Southeast Asia — encompassing India, Pakistan, Bangladesh, Sri Lanka, China, Malaysia, and the Philippines — the plant has been integral to Ayurvedic, Siddha, and Unani medicine for centuries.[22,23] Its common names reflect this extensive cultural presence: Madar or Aak in Hindi, Arka in Sanskrit, and Crown Flower or Giant Indian Milkweed in English.[23]

Botanically, the plant attains a height of up to 2.5 m, with a woody branching stem covered in corky, yellowish-grey bark. The leaves are sessile, decussate, elliptic-oblong with an acute apex, pale green on both surfaces, and densely clothed in fine cottony tomentum; they measure 10–20 cm in length and 3.8–10 cm in width. The bisexual flowers are borne in umbellate lateral cymes and measure 3.8–5 cm in diameter, presenting in white or purple colour with a faint odour. Follicular fruits, 9–10 cm long, contain numerous flat, ovate seeds bearing a silky coma 2.5–3.2 cm in length. The root system comprises a deep, stout taproot with few lateral extensions.[22]

Table 1: Taxonomic Classification of Calotropis procera.

Taxonomic Rank	Classification
Kingdom	Plantae
Order	Gentianales
Family	Apocynaceae
Subfamily	Asclepiadaceae
Genus	Calotropis
Species	C. procera, C. gigantea

Phytochemical Profile

The various organs of Calotropis procera are rich in bioactive secondary metabolites. The bark yields alkaloids, glycosides, carbohydrates, proteins, anthraquinones, phenols, tannins, flavonoids, and sterols. The milky latex is particularly concentrated in cardenolide glycosides including calotropin, calotoxin, calactin, uscharin, and proceroside, which account for many of the plant's pharmacological activities. Collectively, these constituents confer anthelmintic, anticancer, CNS-modulating, anticonvulsant, antipyretic, anti-inflammatory, and antimicrobial properties to various plant parts.[24]

Wound Healing Applications

Topical application of Calotropis procera leaf preparations has been documented in traditional practice for the management of fresh and infected wounds, joint swellings, localized oedema, and cutaneous infections. The latex of the plant exhibits notable antimicrobial efficacy, actively suppressing the growth of wound-associated pathogens such as Staphylococcus aureus and Escherichia coli, thereby preserving the sterility of the

wound environment. Fibroblast-stimulating activity has been attributed to specific glycoside fractions, and in vivo studies using excision wound models have demonstrated significant acceleration in wound closure, improvement in granulation tissue formation, and enhanced epithelial regeneration compared to untreated controls.[24]

4.2 Aegle marmelos (L.) Correa — Bael

Aegle marmelos, commonly known as Bael, belongs to the family Rutaceae and is arguably one of the most therapeutically significant plants in the classical Ayurvedic pharmacopoeia. All parts of the plant — leaves, bark, roots, unripe and ripe fruits — have been employed medicinally, but the fruit has attracted particular scientific attention on account of its remarkable wound healing properties.[25] Traditional Ayurvedic texts document its application in the management of wounds, ulcers, burns, and diverse skin disorders.

Phytochemical Composition

The fruit of Aegle marmelos is notably rich in pharmacologically active phytochemicals. Major identified constituents include marmelosin (a furocoumarin), flavonoids, tannins, alkaloids, phenolic acids, coumarins, terpenoids, and volatile aromatic compounds. These molecules interact in a complementary fashion to produce the broad therapeutic spectrum characteristic of this plant.[25]

Table 2: Wound Healing Mechanisms of Aegle marmelos Fruit.

Mechanism	Active Constituents	Therapeutic Outcome
Antioxidant Activity	Polyphenols, Flavonoids, Coumarins	Neutralization of reactive oxygen species; protection of regenerating tissue from oxidative stress
Antimicrobial Activity	Alkaloids, Tannins, Phenolic acids	Suppression of S. aureus, E. coli, K. pneumoniae, P. aeruginosa; prevention of wound infection
Anti-inflammatory Activity	Flavonoids, Phenolics	Downregulation of pro-inflammatory mediators; reduction of wound-site oedema and erythema
Collagen Synthesis & Fibroblast Stimulation	Marmelosin, Terpenoids	Enhanced hydroxyproline levels; improved granulation tissue organization and tensile strength

Preclinical investigations employing standardized excision and incision wound models have consistently demonstrated that both ethanolic and methanolic fruit extracts of Aegle marmelos significantly accelerate wound contraction and reduce the epithelialization period relative to untreated controls. Histological examination of treated tissues reveals superior collagen alignment, reduced inflammatory cell infiltration, and well-organized scar architecture. The mucilaginous nature of the fruit pulp, traditionally applied as a topical paste on chronic ulcers and infected wounds, additionally contributes by maintaining adequate moisture at the wound surface, limiting desiccation-induced tissue damage.[25]

Contemporary research has begun exploring the integration of Aegle marmelos extracts into advanced wound dressing formulations including ointments, hydrogels, biopolymeric films, and transdermal delivery patches, taking advantage of its favourable safety profile and multifunctional bioactivity.[25]

5. ADVANCED DRUG DELIVERY SYSTEMS FOR LOCALIZED WOUND THERAPY

The incorporation of bioactive herbal agents into purpose-designed drug delivery platforms represents a critical step in translating traditional wound healing knowledge into clinically effective products. Such systems are designed to protect labile phytoconstituents from degradation, achieve sustained therapeutic drug concentrations at the wound site, and minimize systemic absorption. The principal delivery platforms evaluated for wound applications are described below.

5.1 Microspheres and Microcarrier Systems

Microspheres are spherical polymeric particulate systems with diameters spanning 1 to 1000 µm, functioning as injectable cellular scaffolds with a high surface-area-to-volume ratio that facilitates drug loading and controlled release.[26] Their internal architecture can be engineered into macroporous, nanofibrous, hollow, or core-shell configurations to accommodate diverse drug molecules and cell types. For applications involving cellular carriers in tissue engineering, a diameter range of 20–200 µm is considered optimal, since most adherent mammalian cells exceed 20 µm in spread diameter.[26,27]

Despite their versatility, polymer-based microspheres present certain inherent limitations: their compressive moduli are relatively low, restricting applicability in mechanically loaded tissue environments. Moreover, the in vivo stability of microsphere preparations under physiological conditions requires further characterization, and chemical crosslinking — though necessary to prevent diffusion into adjacent tissues — must be optimized to avoid cytotoxicity.[28,29]

5.2 Metal and Metal Oxide Nanoparticles

Nanoparticulate systems fabricated from metals and metal oxides — including silver (AgNPs), gold (AuNPs),

iron oxide (Fe_3O_4), titanium dioxide (TiO_2), and zinc oxide (ZnO) — have emerged as powerful adjuncts in wound infection management, owing to their broad-spectrum bactericidal properties and capacity for simultaneous drug delivery.[30] Silver and gold nanoparticles are the most extensively studied; their unique nanoscale physicochemical attributes — including small size, high surface reactivity, and tunable surface chemistry — endow them with distinct advantages over conventional antibiotics in overcoming resistance mechanisms.[30,31]

Numerous surface engineering strategies have been employed to enhance the antibacterial potency of AgNPs while maintaining acceptable biocompatibility, including encapsulation within lipid micelles, coating with gold shells, and functionalization with N-heterocyclic compounds. These approaches extend the spectrum of bactericidal activity and reduce non-specific cytotoxicity toward host cells, improving the therapeutic index of nanoparticle-based wound treatments.[32,33]

5.3 Hydrogel-Based Wound Dressings

Hydrogels are water-swollen, three-dimensional polymeric networks synthesized from natural macromolecules (chitosan, hyaluronic acid, gelatin) or synthetic polymers (polymethacrylates, polyvinyl pyrrolidone) that retain structural integrity in the swollen state. With water contents of 80–90%, these materials create a wound microenvironment that promotes autolytic debridement, supports gas exchange, and minimizes patient discomfort during dressing changes.[34]

Beyond passive moisture management, functional hydrogels serve as reservoirs for the sustained delivery of growth factors, antibiotics, and herbal bioactives. The integration of pH-sensing elements within hydrogel matrices enables real-time monitoring of wound conditions, since chronically non-healing wounds characteristically display elevated pH values compared to normally healing wounds. This monitoring capacity allows wound care practitioners to tailor therapeutic interventions based on dynamic wound status.[35,36,37]

5.4 Vesicular Carrier Systems

Vesicular drug delivery systems are colloidal structures assembled from amphiphilic molecules that spontaneously form bilayer or multilayer enclosures capable of entrapping hydrophilic drugs in their aqueous core and lipophilic drugs within the bilayer membranes. This structural flexibility makes vesicles uniquely suited to the co-delivery of plant extract components with diverse physicochemical properties.[38]

(a) Conventional Liposomes — Although widely studied for topical drug delivery, conventional liposomes are limited by the barrier properties of the stratum corneum, which restricts their penetration to the outermost skin layers. Notwithstanding this limitation, liposomal encapsulation improves the pharmacokinetic behaviour of antibiotics and herbal actives by reducing systemic toxicity, enhancing target specificity, and prolonging drug residence at the application site.[38,39]

(b) Transferosomes — These are elastically deformable vesicles stabilized by edge-activating surfactants (e.g., sodium cholate, polysorbate 80) that impart sufficient membrane flexibility for the vesicles to squeeze through intercellular channels in the stratum corneum significantly narrower than their own diameter. The driving force for this transdermal permeation is a transcutaneous hydration gradient. Research has consistently demonstrated that transferosomal formulations can deliver poorly bioavailable drugs — including herbal phenolics — into the deeper dermal compartments and even the systemic circulation.[42,43]

(c) Ethosomes — Ethanol-enriched vesicular carriers ranging from 103 to 200 nm in diameter, ethosomes exploit the membrane-fluidizing effect of ethanol to destabilize lipid packing in the stratum corneum, facilitating carrier penetration into deeper skin strata. Comparative studies indicate that ethosomes outperform both conventional liposomes and hydroalcoholic solutions in terms of skin deposition. Ethosomal preparations loaded with silver sulfadiazine, a reference topical antibiotic for burn wound management, have shown enhanced in vitro antibacterial activity and superior in vivo healing outcomes in second-degree burn models.[38,44]

(d) Phytosomes — Phytosomes are phospholipid–phytoconstituent complexes designed to overcome the poor membrane permeability of polyphenolic plant actives by integrating them into a lipid-compatible structural framework. This complexation markedly improves the dermal bioavailability of flavonoids, tannins, and phenolic acids that would otherwise be poorly absorbed through topical application. Phytosomal preparations of wound-active herbal extracts have demonstrated significant antioxidant capacity and tissue-repairing efficacy in preclinical assessments.[44,45,46]

6. GROWTH FACTORS IN WOUND REPAIR

Endogenous growth factors are secreted polypeptides that exert regulatory control over virtually every cellular event in the wound healing cascade, including cell migration, proliferation, differentiation, and extracellular matrix synthesis. The principal growth factors implicated in wound repair are summarized in Table 3.

Table 3: Major Growth Factors in Wound Healing and Their Roles.

Growth Factor	Target Cell Types	Route of Admin.	Key Biological Functions
EGF	Fibroblasts, Keratinocytes	Topical	Promotes cell migration, proliferation, and differentiation; hastens epidermal layer restoration.[47]
PDGF	Neutrophils, Macrophages, Fibroblasts, Smooth muscle cells	Topical	Reinforces vascular integrity; stimulates mitogenic activity, ECM deposition, and epithelial resurfacing.[48]
bFGF	Keratinocytes, Fibroblasts	Topical	Induces collagenase synthesis, extracellular matrix formation, and re-epithelialization.[49]
GM-CSF	Keratinocytes, Endothelial cells, Eosinophils, Macrophages	Subcutaneous / Topical	Mobilizes inflammatory effector cells; supports wound contraction, mitosis, and cellular expansion.[50]
TGF-β	Keratinocytes, Macrophages, Lymphocytes, Fibroblasts	Topical	Directs granulation tissue assembly, epithelial resurfacing, matrix synthesis, and tissue remodelling.[51]

7. CONCLUSION

This review presents a comprehensive synthesis of the scientific evidence supporting the use of Aegle marmelos and Calotropis procera as therapeutically complementary components of polyherbal wound healing formulations. Both plants contribute a complementary and non-overlapping set of bioactivities — antioxidant, antimicrobial, anti-inflammatory, and pro-collagenic — that collectively address the multiple physiological barriers impeding effective wound repair. The substantial body of traditional knowledge surrounding these species continues to be corroborated by contemporary pharmacological research, strengthening the scientific rationale for their combined use in herbal wound care products.

The incorporation of phytoconstituents from these plants into advanced delivery platforms — including vesicular systems, hydrogels, microspheres, and nanoparticulate carriers — offers a pathway to improving bioavailability and achieving sustained therapeutic concentrations at the wound site. The modulatory roles of EGF, PDGF, bFGF, GM-CSF, and TGF-β further highlight the need for formulation strategies that either incorporate or stimulate these endogenous mediators to maximize healing outcomes.

Future research efforts should prioritize the chemical standardization of herbal extracts, detailed mechanistic investigations to identify the specific molecular targets involved, and rigorously designed preclinical and clinical trials to establish the efficacy and safety of the proposed polyherbal formulations. Such research will be essential for integrating these time-honoured Ayurvedic remedies into the evidence-based wound management framework of modern medicine.

ABBREVIATIONS

AgNPs: Silver Nanoparticles; AuNPs: Gold Nanoparticles; bFGF: Basic Fibroblast Growth Factor; CAT: Catalase; CNTs: Carbon Nanotubes; ECM: Extracellular Matrix; EGF: Epidermal Growth Factor; EGCG: Epigallocatechin-3-Gallate; GM-CSF: Granulocyte-Macrophage Colony-Stimulating Factor; HIF-1: Hypoxia-Inducible Factor-1; IGF-1: Insulin-Like Growth Factor-1; IL-1: Interleukin-1; MAPK: Mitogen-Activated Protein Kinase; MMP-1: Matrix Metalloproteinase-1; MRSA: Methicillin-Resistant Staphylococcus aureus; PDGF: Platelet-Derived Growth Factor; pNFκB: Phospho-Nuclear Factor Kappa B; SOD: Superoxide Dismutase; TGF-β: Transforming Growth Factor Beta; TNF-α: Tumour Necrosis Factor Alpha; VEGF: Vascular Endothelial Growth Factor; VPF: Vascular Permeability Factor.

REFERENCES

1. Strodtbeck F. Physiology of wound healing. Newborn and Infant Nursing Reviews, 2001; 1(1): 43–52.
2. Roberts PR, LATG KW, Santamauro JT, Zaloga GP. Dietary peptides improve wound healing following surgery. Nutrition, 1998; 14(3): 266–269.
3. Thomas DR, Kamel HK. Wound management in postacute care. Clinics in Geriatric Medicine, 2000; 16(4): 783–803.
4. Menke NB, Ward KR, Witten TM, Bonchev DG, Diegelmann RF. Impaired wound healing. Clinics in Dermatology. 2007; 25(1): 19–25.
5. Netam AK, Prasad J, Satapathy T. A review on ethnopharmacological approaches to wound healing and curative progression. Research Journal of Pharmacology and Pharmacodynamics, 2019; 11(1): 37–45.

6. Li J, Chen J, Kirsner R. Pathophysiology of acute wound healing. Clinics in Dermatology. 2007; 25(1): 9–18.
7. Stadelmann WK, Digenis AG, Tobin GR. Physiology and healing dynamics of chronic cutaneous wounds. American Journal of Surgery 1998; 176(2): 26S–38S.
8. Madden JW, Peacock JE Jr. Studies on the biology of collagen during wound healing. Surgery, 1968; 64(1): 288–294.
9. Prockop DJ, Kivirikko K, Tuderman L, Guzman N. The biosynthesis of collagen and its disorders. New England Journal of Medicine, 1979; 301: 13–23.
10. Kumar B, Vijayakumar M, Govindarajan R, Pushpangadan P. Ethnopharmacological approaches to wound healing — exploring medicinal plants of India. Journal of Ethnopharmacology, 2007; 114(2): 103–113.
11. Jinich-Diamant A et al. Neural and molecular changes during a mind-body reconceptualization and open-label placebo healing intervention. Communications Biology, 2025; 8(1): 1525.
12. Kanungo J, Sharma J, Patel AK. Wound healing activity of hydroalcoholic extracts of Lycopersicon esculentum and Ficus racemosa on Wistar rats. International Journal, 2024; 9(10): 1–6.
13. Patil S, Ghodke DS, Magdum CS, Naikwade NS. Evaluation of healing activity of marketed formulations on excision wound models in albino rats. Int J Pharm Tech Res., 2009; 1(3): 500–501.
14. Sabale PS, Bhimani BB, Prajapati CP, Sabalea VS. An overview of medicinal plants as wound healers.
15. Chaudhary A, Singh N. Contribution of the World Health Organization to the global acceptance of Ayurveda. Journal of Ayurveda and Integrative Medicine, 2011; 2(4): 179.
16. Zahin F, Aqil I, Ahmad I. Total phenolic content and antioxidant activity of four Indian medicinal plants. International Journal of Pharmacy and Pharmaceutical Sciences, 2012; 2(3): 286–304.
17. Bamola N, Verma P, Negi C. A review on some traditional medicinal plants. International Journal of Life-Sciences Scientific Research, 2018; 4(1): 1550–1556.
18. Jamshidi-Kia F, Lorigooini Z, Amini-Khoei H. Medicinal plants: past history and future perspective. Journal of Herbmed Pharmacology, 2017; 7(1): 1–7.
19. Gupta DM, Longaker MT. Tissue Engineering for the Hand: Research Advances and Clinical Applications, 2010: 195.
20. Atiyeh BS, Amm CA, El Musa KA. Improved scar quality following primary and secondary healing of cutaneous wounds. Aesthetic Plastic Surgery, 2003; 27(5): 411–417.
21. Yadav KN, Kadam PV, Jagdale SK, Patil MJ. Herbal remedy for wound management: a review. International Journal of Pharmacognosy, 2018; 5(8): 440–449.
22. Kumar PS, Chezhian A, Raja PS, Sathiyapriya J. Computational selections of terpenes present in Calotropis gigantea as mosquito larvicide. Bangladesh Journal of Pharmacology, 2012; 7(1): 1–5.
23. Pophale SP, Mokle BA, Sanap G. Review article on Calotropis gigantea. Inter J Creativ Res Thoughts, 2023; 11(3): 566–587.
24. Kokate CK, Purohit A, Gokhale S. Practical Pharmacognosy. Vallabh Prakashan, New Delhi, 1994: 54.
25. Punjaji SA. Some less known herbal remedies against cut and wounds from Ahmednagar, Maharashtra, India. Int. J. Basic Appl. Sc., 2012; 1: 184–197.
26. Huang S, Lu G, Wu Y et al. Mesenchymal stem cells in microsphere-based engineered skin for wound healing. Journal of Dermatological Science, 2012; 66(1): 29–36.
27. Li H, Wang F. Core-shell chitosan microsphere with antimicrobial and vascularized functions for wound healing. Materials and Design. 2021; 204: 109683.
28. Zhang D, Ouyang Q, Hu Z et al. Catechol-functionalized chitosan/active peptide microsphere hydrogel for skin wound healing. International Journal of Biological Macromolecules, 2021; 173: 591–606.
29. Negut I, Grumezescu V, Grumezescu AM. Treatment strategies for infected wounds. Molecules, 2018; 23(9): 2392.
30. Jahromi MA, Zangabad PS, Basri SM et al. Nanomedicine and advanced technologies for burns. Advanced Drug Delivery Reviews, 2018; 123: 33–64.
31. Negut I, Grumezescu V, Grumezescu AM. Treatment strategies for infected wounds. Molecules, 2018; 23(9): 2392.
32. Jahromi MA et al. Nanomedicine for burns. Advanced Drug Delivery Reviews, 2018; 123: 33–64.
33. Likus W, Bajor G, Siemianowicz K. Nanosilver — does it have only one face? Acta Biochimica Polonica, 2013; 60(4).
34. Alven S, Aderibigbe BA. Chitosan and cellulose-based hydrogels for wound management. International Journal of Molecular Sciences, 2020; 21(24): 9656.
35. Kharaziha M, Baidya A, Annabi N. Rational design of immunomodulatory hydrogels for chronic wound healing. Advanced Materials, 2021; 33(39): 2100176.
36. Roy N, Saha N, Humpolicek P, Saha P. Permeability and biocompatibility of medicated hydrogel wound dressings. Soft Materials, 2010; 8(4): 338–357.
37. Reimer K, Fleischer W, Brögmann B et al. Povidone-iodine liposomes — an overview. Dermatology, 1997; 195(Suppl. 2): 93–99.
38. Xu HL, Chen PP, ZhuGe DL et al. Liposomes with silk fibroin hydrogel core to stabilize bFGF and

promote wound healing. Advanced Healthcare Materials, 2017; 6(19): 1700344.
39. Reimer K et al. Povidone-iodine liposome hydrogel for wound healing. Dermatology, 2000; 201(3): 235–241.
40. Reimer K et al. Topical drug formulation for wound healing. Dermatology, 2000; 201(3): 235–241.
41. Sağıroğlu AA, Çelik B, Güler EM et al. Wound healing potential of composite liposomal films. Pharmaceutical Development and Technology, 2021; 26(4): 444–454.
42. Xu HL et al. Liposomes for wound healing of deep second-degree scald. Advanced Healthcare Materials, 2017; 6(19): 1700344.
43. Sağıroğlu AA et al. Composite liposomal films for wound healing. Pharmaceutical Development and Technology, 2021; 26(4): 444–454.
44. Sağıroğlu AA et al. Wound healing evaluation of liposomal combination films. Pharmaceutical Development and Technology, 2021; 26(4): 444–454.
45. Santos AC, Rodrigues D, Sequeira JA et al. Nanotechnological breakthroughs in topical phytocompound-based formulations. International Journal of Pharmaceutics, 2019; 572: 118787.
46. Shakeel F, Alam P, Anwer MK et al. Wound healing of self-nanoemulsifying drug delivery containing Piper cubeba essential oil. 3 Biotech., 2019; 9(3): 82.
47. Fisher DA, Lakshmanan J. Metabolism and effects of epidermal growth factor in mammals. Endocrine Reviews, 1990; 11(3): 418–442.
48. Lindahl P, Johansson BR, Levéen P, Betsholtz C. Pericyte loss in PDGF-B-deficient mice. Science, 1997; 277(5323): 242–245.
49. Dickson C, Spencer-Dene B, Dillon C, Fantl V. Fibroblast growth factors and their receptors in breast cancer. Breast Cancer Research, 2000; 2(3): 191.
50. Gabrilove JL et al. Effect of granulocyte colony-stimulating factor on neutropenia due to chemotherapy. New England Journal of Medicine, 1988; 318(22): 1414–1422.
51. Huang JS, Wang YH, Ling TY et al. Synthetic TGF-β antagonist accelerates wound healing and reduces scarring. The FASEB Journal, 2002; 16(10): 1269–1270.