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A Review Plant- Derived Wound Healing Agents in Diabetic Ulcer Management

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ABSTRACT
Impaired insulin function and persistent hyperglycemia are hallmarks of diabetes mellitus (DM), a chronic metabolic disease that frequently results in serious side effects such neuropathy, blindness, and diabetic foot ulcers (DFUs). One of the most dangerous and difficult side effects of diabetes is diabetic foot ulcers (DFUs), which can often lead to infection, delayed wound healing, or even amputation. Traditional treatment approaches, such as the use of antibiotics, bandages, and surgery, are frequently expensive and constrained by tissue regeneration issues and antibiotic resistance. As a result, chemicals derived from plants are receiving more attention as viable substitutes for accelerating the healing of diabetic ulcers.
Curcuma longa, Aloe barbadensis, Carica papaya, Persea americana, Leptospermum scoparium, Curculigo orchioides, Martynia annua, Rosmarinus officinalis, Vitis vinifera, and Actinidia deliciosa are only a few of the medicinal plants whose therapeutic potential is highlighted in this analysis. Flavonoids, tannins, phenolics, and essential oils are examples of bioactive components found in these plants that have angiogenic, antibacterial, anti-inflammatory, and antioxidant properties. These natural agents speed up tissue healing and lessen oxidative stress through processes like collagen production, fibroblast proliferation, re-epithelialization, and increased VEGF expression. Thus, including plant-based treatments into contemporary diabetic wound care procedures provides a secure, cost-effective, and biocompatible method that can boost patients' quality of life and promote healing results.

I. INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disease caused by insufficient insulin secretion or absorption, leading to abnormal blood glucose regulation. The global prevalence of DM has risen significantly due to factors such as obesity, inactivity, aging, and genetic predisposition. Neglecting this condition results in several complications, including neuropathy, retinopathy, endothelial dysfunction, atherosclerosis, and diabetic foot ulcers (DFUs). DFUs are among the most serious and common complications, affecting nearly 15% of diabetic patients and representing a leading cause of non-traumatic lower-limb amputations (Nilforoushzadeh et al., 2012 [1]; Powlson & Coll, 2011[2]; Tentolouris et al., 2004[3]). These ulcers are difficult to heal and impose a heavy burden on patients and healthcare systems.

Various therapeutic approaches, including antibiotics, neuropathic medications, and biomedical devices, have been used to manage DFUs and enhance wound healing. However, many infections have become resistant to antibiotics, requiring frequent and high doses, while medical devices demand skilled professionals and costly hospitalization. Since DFU results from multiple underlying disorders, single-approach treatments often show limited success. This has led to increased interest in alternative therapies—particularly herbal medicines—that are biocompatible, biodegradable, and less toxic (Kumar et al., 2007[4]).

Traditional Indian medicine, such as Ayurveda, describes numerous natural remedies with wound-healing properties, collectively referred to as "Vranaropaka." Many medicinal plants possess bioactive compounds with antioxidant and tissue-regenerative properties, supporting all phases of wound repair. Antioxidants from herbs can neutralize reactive oxygen species (ROS), helping to prevent oxidative stress-related damage common in diabetic wounds. By providing essential nutrients like vitamins, proteins, and minerals, herbal extracts accelerate tissue regeneration and healing (Kumar et al., 2007 [4]; Nilforoushzadeh et al., 2012 [1]).

In recent years, medicinal plants have gained renewed scientific interest for their potential to manage diabetic wounds effectively. Clinical studies have shown encouraging results—for

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instance, herbal formulations have helped prevent limb amputation in DFU patients (Tentolouris et al., 2004[3]). As a result, researchers are increasingly exploring plant-derived molecules for their wound-healing effects, viewing herbal medicine as a safe, affordable, and promising alternative to conventional therapies in the management of diabetic complications, especially DFUs (Powlson & Coll, 2011[2]; Kumar et al., 2007[4]).

CURCUMA LONGA

MECHANISM

`Curcuma longa, or turmeric Turmeric is a member of the Zingiberaceae family. Curcumin, desmethoxycurcumin, and bis-desmethoxycurcumin are its main components. It reduces inflammation by decreasing the activity of TNF-α, IL-1, and NF-κB cytokines. Additionally, it promotes wound healing by increasing fibroblast migration, proliferation, granulation tissue development, and collagen deposition. [10,13,17]

1. Synonyms	Turmeric, Haldi, Haridra [5]
2. Biological Source	Dried rhizomes of Curcuma longa Linn.[5,6]
3. Family	Zingiberaceae[5]
4. Chemical Constituents	Curcuminoids (Curcumin – 77%, Demethoxycurcumin, Bisdemethoxycurcumin)[7] – Volatile oils (turmerone, atlantone, zingiberene)[7,8] – Proteins, sugars, and resins[6]
5. Uses	–Dietary spices and coloring agents (traditional use) [5] – Antibiotic and anti-infective (prevents bacterial infection of injured tissue) [9] – Anti-inflammatory (lowers inflammation by inhibiting TNF-α and IL-1 cytokines) [10,11] – Antioxidant: lowers oxidative stress and scavenges free radicals [12] – Wound healing (improving granulation tissue production, collagen deposition, and tissue remodeling) [13,14] – Anti-diabetes, anti-cancer, and anti-aging (particularly helpful in diabetic wound healing) [15,16] In wounds, it stimulates fibroblast growth and epithelial renewal.[13]

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AVACADO

MECHANISM

Avocado (Persea americana) belongs to the Lauraceae family. Monounsaturated fatty acids, lutein, vitamins A and E, phospholipids, and glycolipids are among its principal components [19,20,23]. By encouraging the production of collagen and supplying vital nutrients including proteins, fatty acids, and potassium, it aids in the healing of wounds [22,23]

1. Synonyms	Avocado, Alligator Pear, Butter Fruit
2. Biological Source	Fruit pulp of Persea americana Mill
3. Family	Lauraceae
4. Chemical Constituents	Monounsaturated fatty acids (oleic acid) [19,23] Carotenoids (mainly lutein – 70% of total carotenoids) [19,20,23] Vitamins: A and E [19,23] Phospholipids and glycolipids [19,20] Flavonoids [18,20] Minor components: saponins, sterols [18,21]
5. Uses	Wound healing: Encourages angiogenesis, collagen synthesis, fibroblast proliferation, and epithelialization [22] Antioxidant: Because of the presence of flavonoids, carotenoids, and vitamin E [19,20,23] Anti-inflammatory: Prevents platelets from synthesizing prostaglandins [23] Antifungal and antibacterial: Effective against specific infections [21] Hepatoprotective: Shields liver cells from harmful substances [20,23] Vasorelaxant: Inhibits Ca^{2+} mobilization to induce smooth muscle relaxation [23] High levels of lutein and antioxidants have the ability to prevent cancer [19,20,23]

ALOE VERA

MECHANISM

Aloe vera, or Aloe barbadensis[24,25,26]. Aloe vera belongs to the family Xanthorrhoeaceae.[24,25] It includes sterols, triterpenoids, anthraquinones, naphthoquinones, and saponins[25,26,27]. These substances have antibacterial and bacteriostatic properties, improve blood flow to the lesion, and lessen pain and inflammation[25,27,28].

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1.	Synonyms	Aloe vera, Kumari, Ghritkumari
2.	Biological Source	Gel obtained from the leaves of Aloe barbadensis Mill[24,25]
3.	Family	Xanthorrhoeaceae (formerly Liliaceae)[24,25]
4.	Chemical Constituents	Polysaccharides: Glucomannan, Acemannan, Mannose-6-phosphate [25,26] Anthraquinones: Aloin, Emodin [24,25] Saponins [24,25] Naftoquinones [25,27] Sterols and Triterpenoids [24,26] Gibberellin (plant growth hormone) [26] Enzymes: Carboxypeptidase, Bradykinase [24,25]
5.	Uses	Wound healing: Promotes collagen synthesis, fibroblast proliferation, and epithelialization [25,27,28] Anti-inflammatory: Inhibits prostaglandins and bradykinin to reduce pain and inflammation [24,25,27] Antibacterial: Prevents wound infection because of anthraquinones [25,28] Antioxidant: Promotes tissue regeneration and repair [26,27] Strengthens scars and increases collagen cross-linking [25,27] Encourages the production of granulation tissue and the contraction of wounds [25,27,28] Utilized in the treatment of diabetic ulcers and wounds [25,28]

PAPAYA

MECHANISM

Papaya (Carica papaya) belongs to the Caricaceae family. Monounsaturated fatty acids, lutein, vitamins A and E, phospholipids, and glycolipids are among its principal components. By encouraging the production of collagen and supplying vital nutrients including proteins, fatty acids, and potassium, it aids in the healing of wounds. [29,30,34]

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1.	Synonyms	Papaya, Pawpaw, Papita
2.	Biological Source	Fruit, latex, and seeds obtained from Carica papaya Linn.[29,30]
3.	Family	Caricaceae[30,31]
4.	Chemical Constituents	Enzymes: Papain, Chymopapain [29,32] Flavonols, Nicotine, Tannins, Terpinenes [31,33] Alkaloids and Saponins (minor components) [31,33] Amino acids such as proline and hydroxyproline precursors [29,34]
5.	Uses	Wound healing: Encourages granulation tissue growth, epithelialization, and collagen production [30,33] Debridement agent: Papain and chymopapain are enzymes that aid in the removal of dead tissue and promote healing. [32,34] Antibacterial: Effective against Bacillus cereus, Shigella flexneri, Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus[30,33] Antidiabetic/Hypoglycemic: Promotes better healing of diabetic wounds and lowers blood glucose levels [31,33] Anti-inflammatory: Lowers injured tissue inflammation [29,30] Historically, it has been used to treat infections, diabetes, and obesity. [31]

MANUKA HONEY

MECHANISM

Manuka honey, or Leptospermum scoparium. The active ingredient in manuka honey, which belongs to the Myrtaceae family, is methylglyoxal. It possesses debridement qualities that aid in wound cleaning and exhibits potent antibacterial action against MRSA (Methicillin- resistant Staphylococcus aureus). [35,36,41]

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1.	Synonyms	Manuka Honey, Monofloral Honey
2.	Biological Source	Honey obtained from the nectar of Leptospermum scoparium (Manuka tree)[35,36]
3.	Family	Myrtaceae[35]
4.	Chemical Constituents	Methylglyoxal (MGO) – main active antibacterial component [35,37] Hydrogen peroxide (minor antibacterial factor) [36] Phenolic compounds and Flavonoids [35,37] Sugars (glucose, fructose, sucrose) [35] Amino acids (arginine, lysine, cysteine) [35] Organic acids and enzymes [35]
5.	Uses	Wound healing: Encourages tissue repair, creates a moist environment, and speeds up closure [38,39] Methylglyoxal's potent antibacterial action effectively combats a wide range of microorganisms [35,36] Anti- inflammatory: Reduces pain and swelling, modifies inflammatory response [35,38] Antioxidant: Promotes healing and neutralizes free radicals [37,39] Immune modulator: Boosts immunity and lowers the risk of infection [39] The US FDA approved it in 2007 for the treatment of wounds. [36,40] Reduces scarring and relieves diabetic ulcer discomfort. [38,40]

CURCULIN

MECHANISM

Curculin, or Curculigoorchioides. Curculin is a member of the family Hypoxidaceae. Curculigosides, flavonoids, tannins, and phenolic compounds are some of its main components. It prevents lipid peroxidation in granulation tissue by acting as a free radical scavenger with antibacterial qualities. [47,42]

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1. Synonyms	Curculin, Golden Eye-grass, Kali Musli
2. Biological Source	Root tubers of Curculigo orchioides Gaertn.[42,43]
3. Family	Hypoxidaceae[43,44]
4. Chemical Constituents	Flavonoids (antioxidant and free radical scavenging) [45,42] Tannins (astringent, antimicrobial, free radical scavenger) [42,45] Saponins (antioxidant and antimicrobial) [42,44] Phenolic compounds [42,45] Triterpenoids [46,42]
5. Uses	Wound healing: Encourages the production of granulation tissue, angiogenesis, and re-epithelialization [47,42] Antioxidant: Lowers lipid peroxidation and raises nitric oxide and superoxide dismutase levels [47,45] Antimicrobial: Prevents infections in wounds [45,42] Anti-inflammatory: Lowers tissue inflammation and oxidative stress [46,45] When used in diabetic wound healing, it improves tissue repair and wound contraction. [47,42] In Ayurveda, it is traditionally used as an aphrodisiac, revitalizing herb, and tonic. [43,44]

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MARTYNIA

MECHANISM

Martynia annua. This plant is a member of the family Martyniaceae. Steroids, palmitic acid, oleic acid, arachidic acid, and chlorogenic acid are all present. Oxidative stress is inhibited by it. This plant contains luteolin, which has double the antioxidant capacity of vitamin E and aids in the neutralization of superoxide radicals. [48,50]

1.	Synonyms	Martynia, Devil's Claw, Tiger's Claw, Kaknasa
2.	Biological Source	Whole plant or aerial parts of Martynia annua Linn.[48,49]
3.	Family	Martyniaceae[49,50]
4.	Chemical Constituents	Flavonoids (especially Luteolin) [48,50] Glycosides [49,50] Tannins [48,51] Carbohydrates [49,50] Phenolic compounds [48,51] Anthocyanins [50,51]
5.	Uses	Promotes angiogenesis, fibroblast proliferation, and collagen production [48,49] Antioxidant: Luteolin is twice as effective in scavenging free radicals as vitamin E [48,52] Anti-inflammatory: Lowers oxidative stress and wound inflammation [51,49] Antibacterial: Prevents infection in tissue that is healing [50,48] Promotes quicker wound contraction and tissue repair when used in diabetic wound healing. [49,48] Traditional use: Known for treating inflammatory and skin conditions [50,48]

ROSEMARY

MECHANISM

Rosemary, or Rosmarinus officinalis. Rosemary is a member of the Lamiaceae family. Rosmarinic acid and carnosic acid are its active ingredients. It increases angiogenesis and collagen deposition, aids in wound contraction, aids in re-epithelialization, and lessens inflammation. [53,54]

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1.	Synonyms	Rosemary, Gulmehndi
2.	Biological Source	Leaves and flowering tops of Rosmarinus Officinalis Linn.[53,54]
3.	Family	Lamiaceace[53,54]
4.	Chemical Constituents	Caffeic acid and Rosmarinic acid (major constituents) [54,55] Carnosic acid and Carnosol [53,55] Flavonoids (e.g., luteolin, apigenin) [55,53] Essential oils (camphor, cineole, borneol, pinene) [53,56] Phenolic diterpenes [55,54]
5.	Uses	Wound healing: Encourages angiogenesis, collagen deposition, granulation tissue development, and re-epithelialization [54,53] Antioxidant: Uses carnosic acid and caffeic acid to prevent damage from free radicals. [55,53] Anti-inflammatory: Lowers oxidative stress and tissue inflammation [53,56] Neuroprotective: Prevents brain aging and improves memory and focus [56] Anticancer and vision-protective: Prevents oxidative cellular damage and macular degeneration [55,54] When applied to diabetic wounds, it speeds up tissue regeneration and wound contraction. [54,56]

GRAPE SEED EXTRACT

MECHANISM

Grape Seed Extract from Vitis vinifera (extract from grape seeds) — Oligomeric procyanidins are found in grape seed extract, which belongs to the Vitaceae family. By stimulating vascular endothelial growth factor (VEGF), it speeds up the repair of damaged skin. [57,58]

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1.	Synonyms	Grape Seed Extract, Vitis Extract, Seed of Wine Grape
2.	Biological Source	Extract obtained from the seed of Vitis vinifera Linn.[57,58]
3.	Family	Vitaceae[57,58]
4.	Chemical Constituents	Proanthocyanidins (Oligomeric procyanidins) – main active constituents [57,59] Flavonoids [57,59] Vitamin E [58,59] Linoleic acid [59] Phenolic compounds (polyphenols, tannins) [57,58] α-glycosidase enzyme [58]
5.	Uses	Wound healing: Encourages angiogenesis, VEGF expression, and collagen synthesis [57,58] Antioxidant: More potent than vitamins C and E at scavenging free radicals [59] Anti-inflammatory: Lowers inflammation and oxidative stress in wound tissue [57,58] Antidiabetic: Reduces blood sugar, postpones the absorption of carbohydrates, and enhances microcirculation [58,59] Neuroprotective: Increases the speed at which motor nerves conduct [59] Cardioprotective: Used to prevent vascular damage and atherosclerosis [58,59] Prevents cataracts and gastric ulcers, protecting the eyes and stomach mucosa. [58] Improves diabetic patients' wound healing by lowering blood viscosity and boosting tissue nutrition delivery. [57,58]

CHINESE GOOSEBERRY

MECHANISM

Actinidia deliciosa, or kiwi fruit — The Actinidiaceae family includes kiwi fruit. Along with ascorbic acid, it is high in lutein, fisetin, β-carotene, and vitamins C, E, and K. Its antibacterial and protein-dissolving (debridement) qualities promote skin regeneration and wound healing. [61,60]

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1.	Synonyms	Chinese Gooseberry, Kiwifruit
2.	Biological Source	Fruit obtained from Actinidia deliosa (A. Chev.) C.F. Liang et A.R.[60,61]
3.	Family	Actinidiaceae[60,62]
4.	Chemical Constituents	Vitamins: C, E, K [60,63] Carotenoids: β-carotene (provitamin A), lutein, zeaxanthin [62,63] Proteolytic enzyme: Actinidin [62,64] Ascorbic acid [60,63] Antibacterial and antioxidant compounds [62,64]
5.	Uses	Wound healing: Encourages the production of granulation tissue, collagen, and angiogenesis. [61,64] Debridement agent: Actinidin aids in the breakdown of proteins and the cleansing of wounds. [61,62] Antibacterial: Prevents wound infection [4][1] Antioxidant: Protects tissues by scavenging free radicals [62,63] Increases vascularization and tissue regeneration when used to treat diabetic foot ulcers (DFUs). [60,61]

II. CONCLUSION

The monitoring and treatment of diabetic foot ulcers (DFUs) remain a major problem for medical professionals. Even with the availability of sophisticated wound care methods and drugs, many ulcers are still resistant to traditional treatments, which results in protracted treatment times and subpar healing. Additionally, many patients find DFU treatment to be financially stressful because to the expense of long-term care, many doctor appointments, and the usage of specialist dressings and medicines. The use of herbal medicines as a supplemental or alternative strategy for the treatment of DFUs has received more attention in recent years. Compared to many synthetic medications, these herbal formulations are thought to be promising due to their safer pharmacological profiles, increased affordability, broad availability, and less chance of negative side effects.

Furthermore, many medicinal plants have bioactive chemicals that have anti-inflammatory, antibacterial, antioxidant, and wound-healing qualities. These compounds can speed up tissue regeneration and lower the risk of infection. Herbal remedies frequently work through several biological pathways, improving the entire process of wound healing, in contrast to conventional allopathic pharmaceuticals that typically act on specific molecular targets. In addition to

accelerating healing, this multi-target method aids in enhancing circulation, lowering oxidative stress, and repairing the integrity of the skin. Therefore, the best way to address the ongoing problems with DFU treatment and enhance patients' quality of life may be to incorporate herbal medicines as an alternate or adjunct therapy.

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