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Review Article

Modern Review On Diabetic Wound Healing Potential Of Some Medicinal Herbs

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ABSTRACT

Injuries pose a significant challenge to healthcare in developing nations with limited resources. Approximately 80% of individuals in underdeveloped Nations depend on traditional medicines, predominantly sourced from therapeutic plants, for primary healthcare. In regions like Africa, where traditional knowledge about wound healing is abundant, many people utilize medicinal plants to address diabetic wounds and associated issues. The vast reservoir of medicinal plants in these areas serves as a valuable resource for healthcare solutions. Integrating traditional practices with modern healthcare approaches can be crucial in addressing health challenges, especially in contexts where access to conventional medical resources is constrained. Both internal and external biological organs undergo intricate wound healing processes involving efficient cell-to-cell communication. The stages include haemostasis, inflammation, proliferation, and remodelling, exhibiting high control and organization. By 2040, the global diabetic population is projected to surpass 650 million. Vascular issues and the impaired wound-healing mechanisms associated with diabetes drive increased morbidity and mortality. Understanding and addressing these complex processes are crucial in developing effective strategies for managing diabetic wounds and mitigating the broader health impacts of diabetes on a global scale. This review explores various strategies for treating diabetic wounds, with a particular focus on the international interest in using medicinal plants. It examines factors influencing wound healing in diabetics, the impact of medicinal plants on this process, and the underlying mechanisms of action employed by these plants.

INTRODUCTION

Diabetes is a complicated condition disease resulting from abnormal glucose sensing or insulin

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secretion. In type 2 diabetes, there's Not enough to offset peripheral insulin resistance, while type 1 diabetes involves β-cell death driven by the immune system.1,2,3 Failure to control glucose regulation leads to hyperglycaemia, establishing a significant link between diabetes and its consequential effects..4 Two perilous complications of diabetes, hyperglycaemia, and dyslipidemia, significantly contribute to the advancement of secondary issues, including macro- and micro-vascular problems.5 Hyperglycaemia is primarily responsible for increased protein glycosylation, while glucose oxidation generates free radicals. These radicals can damage cellular membranes by oxidizing low-density lipoproteins or promoting lipoperoxidation of membrane lipids.6,7 Diabetes is on the rise across the African continent, influenced by various factors. The increased morbidity and mortality associated with diabetes result from the emergence of micro- and macrovascular complications and the impairment of the wound-healing mechanism.8,9 Managing diabetic wounds in a clinical setting poses significant challenges due to their slow healing, difficulty in maintenance, and prolonged persistence. The precise pathophysiology contributing to poor wound healing in diabetes wounds remains unclear. However, both human and animal research indicates damage at various stages of the process of healing wounds. Understanding these complexities is necessary for developing effective interventions to enhance the healing of diabetic wounds.10,11 Subsequently, there is a disruption in the composition and functionality of the normal tissue beneath the injury.12,13 A disruption in the skin's cellular, anatomical, and functional integrity brought on by physical, chemical, thermal, microbiological, or immunological assaults is referred to as an injury. Coordinating various cells, growth factors, and cytokines is crucial for completing the repair process.14,15 The precise mechanisms causing slower wound healing in diabetic patients remain unclear. The proliferative phase of the healing process is linked to reduced angiogenesis, impaired epithelium development, and delayed collagen synthesis.16,17 Delayed wound healing in diabetes is associated with reduced vascular endothelial growth factor (VEGF) production, heightened protease activity, delayed inflammatory response, and inadequate nitric oxide generation. These elements have a part in the slowed healing process seen in diabetic wounds.18,19 Inadequate control of wound healing can escalate to the progression of diabetic ulcers on the feet, and in resource-limited settings, may even lead to amputation. This underscores the critical need for accessible and effective therapies to address diabetic-related wound complications.20,21

The Healing Process of Wounds

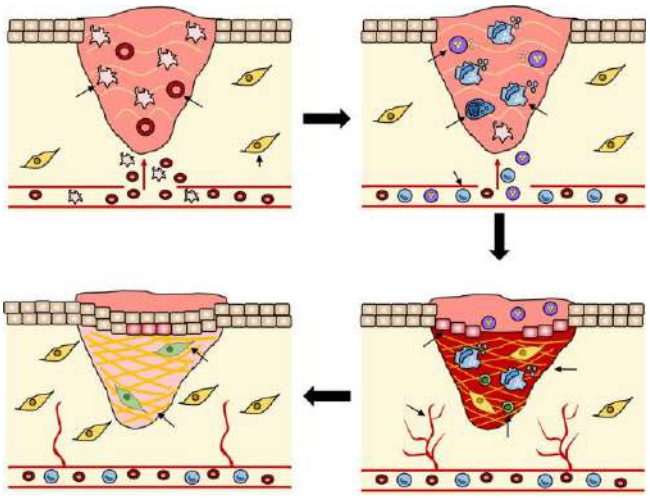

Figure 1. The phases of wound healing and the main cells that make them up.

In addition to performing numerous vital homeostatic tasks, such as controlling thermostability and detecting external stimuli, our skin is specially designed to interact with the outside world. Above all, The body first line of defence is the skin, protecting internal tissues from mechanical, chemical, thermal, and photochemical deterioration as well as desiccation.22,23 The host-microbiota axis, an admirably evolved

mechanism, supports commensal microorganisms while providing protection against pathogenic infection through a complex immune barrier response. In a process known as the wound healing response, the skin has also developed quick and effective mechanisms to seal off breaches in its barrier. The four basic stages of wound repair—haemostasis, inflammation, proliferation, and dermal remodelling—lead to the restoration of both architecture and physiology.24,25

Medicinal Plants Function in the Healing of Wounds in Diabetic Model

The ethnobotanical survey has identified numerous plant and herb species with wound-healing properties. Using medicinal herbs to treat wounds include debridement, cleansing, and establishing an atmosphere that promotes the body's natural healing process. The interest in using medicinal plants for wound healing, in both diabetes and non-diabetic diseases, is growing due to the assumption that their constituents are less toxic and have fewer adverse effects than standard therapeutic treatments.26,27 Health professionals globally recognize impaired wound healing in diabetes as a significant health challenge often attributed to non-specific causes. In response, one therapeutic approach involves the application of medicinal plants, particularly in regions with limited resources.28

Aloe vera

In India, aloe vera, known as Kumari, is a widely used natural remedy. Thriving in the deserts of India, aloe vera is recognized for its medicinal properties, commonly applied in traditional remedies for various health issues due to its soothing and healing attributes.29 Aloe vera comprises over a hundred active ingredients. Additionally, aloe vera has wound-healing abilities. In a model of excision wounds, research by Saini et al. found that Aloe vera leaf pulp outperformed Povidone Iodine ointment (5 percent w/w) in terms of faster and more effective wound healing.30,31 Aloe vera is reported to not only accelerate wound healing but also prevent microbial infections in the affected area. Studies suggest that aloe vera increases lysyl oxidase levels, facilitating cross-linking of newly formed collagen and enhancing collagen turnover rates. Internally consumed, aloe vera is believed to have ulcer-healing properties and skin-protective effects.32,33 Aloe vera gel use topically has been shown to significantly enhance wound contraction and closure. Aloe vera gel influences the level of collagen, a crucial protein in the wound healing process. Studies on histology show that aloe vera gel quickens wound contraction, neo-vascularization, and epithelialization in the later stages of the process of a wound healing.34,35 The medicinal qualities of Aloe vera are attributed to glucomannan, a polysaccharide-based substance.36,37

Figure 2. Aloe vera

Tulsi

The entire Ocimum sanctum, belonging to the Labiaceae family, is prevalent in subtropical and tropical regions of India. Traditionally, various parts of the plant have been utilized in Ayurvedic and Siddha systems to address diverse health issues, including infections, skin conditions, liver problems, and as a remedy for scorpion stings and snake bites.38,39 Ocimum sanctum leaves contain volatile oil along with alkaloids, glycosides, saponins, and tannins, including gallic acid and chlorogenic acid. The composition also includes

70% eugenol, carvenol, and eugenol-methyl ether.40 Ocimum sanctum compounds primarily protect against cellular damage by scavenging free radicals.41,42 Ocimum sanctum is essential to the healing of wounds because it actively participating in multiple immunological mechanisms, including antibody generation, the release of hypersensitive reaction mediators, and the tissue's reaction to these mediators at target sites. Additionally, Ocimum sanctum exhibits properties such as enhanced gastrointestinal mucosal defence, antisecretory effects, and protection against gastroduodenal ulcers.43,44 Wound healing is attributed to the volatile oil and aromatic chemicals present in Ocimum sanctum leaves. Products containing Ocimum sanctum during the wound-healing stage show elevated TNF-alpha levels. The flavonoids in Ocimum sanctum, identified through phytochemical screening, contribute to free radical scavenging. Abundant and widely available, Ocimum sanctum serves as a potentially cost-effective treatment for wound care, functioning as a skilled healer and controller of aberrant healing.45,46

Figure 3. Tulsi

Hibiscus rosa-sinensis

Hibiscus rosa-sinensis is a glabrous shrub in the family Malvaceae. Plant exhibits various medical benefits, including anticancer, antihypertensive, antioxidant, and antiammonemic effects. Both leaves and blossoms contribute to hair development and ulcer healing. Additionally, research indicates that flowers possess antifertility properties and are effective in treating arterial hypertension.47,48 The ethanolic extract demonstrated wound-healing properties in Sprague Dawley rat models. When administered at 120 mg/kg per day in water to drink, the extract improved wound contraction, epithelialization, hydroxyproline concentration, granulation tissue, and skin-breaking strength.49,50 Ointments containing 5 and 10 percent w/w of the extract were also investigated in Wistar rat models, showing promising effects on excision, incision, and dead space wounds. The ethanolic extract of H. rosa-sinensis flowers demonstrated wound-healing properties in Sprague Dawley rat models involving excision, incision, and dead space. When administered at 120 mg/kg per day in drinking water, the extract enhanced wound contraction, epithelialization, hydroxyproline concentration, granulation tissue, and skin-breaking strength. Ointments containing different percentage of doses of extract were also investigated in Wistar rat models, showing promising effects. In excision wounds, the extract improved wound contraction and epithelization while also increasing cellular proliferation and collagen formation.51,52 In the incision wound model, it increased the wound breaking strength. The extract raised the hydroxyproline concentration and weight of granulation tissue in the dead space wound. In a different investigation, the ability of an ethanolic extract of H. rosa-sinensis leaf to cure wounds in Wistar rats was assessed. In both the excision and burn wound models, the extract improved wound contraction and epithelialization. The ethanolic extract demonstrated wound-healing properties in Sprague Dawley rat models involving excision, incision, and dead space. When infused into drinking water at a daily dose of 120 mg/kg, the extract enhanced wound contraction,

epithelialization, hydroxyproline concentration, granulation tissue, and skin-breaking strength.53,54 In excision wounds, the extract improved wound contraction and epithelization while also increasing cellular proliferation and collagen formation. The extract raised the hydroxyproline concentration and weight of granulation tissue in the dead space wound. In a different investigation, the ability of an ethanolic extract of leaf to cure wounds in Wistar rats was assessed.55,56 Recently, the N-butyl alcohol extract of H. rosa-sinensis flower was tested on rats with excision wound models. Histological examination revealed the restoration of the skin's natural architecture.57 Staining techniques showed the distribution of collagen, fibroblasts, and epithelium. Immunohistochemical analysis demonstrated increased TGF-β1 and VEGF, indicating involvement in angiogenesis and collagen fibre production.58,59

Figure 4. Hibiscus rosa-sinensis

Anthocephalus cadamba

Anthocephalus cadamba, frequently referred to as Kadamba and belonging to the Rubiaceae family. It is also recognized for its hepatoprotective, wound-healing, and antioxidant properties.60,61 The Ayurvedic literature describes Anthocephalus cadamba for its pharmacological qualities, including anti-diarrhea, detoxifying, pain relief, and effects on seminal fluids. Traditional medicine often employs an aqueous extract of the leaf of Anthocephalus cadamba to address conditions like menorrhagia, discomfort, swelling, and wounds.62,63 The bark decoction of Anthocephalus cadamba is not only beneficial for skin infections but can also be used to address colitis, diarrhea, and dysentery. An alcoholic extract of Anthocephalus cadamba stem bark has demonstrated antidiabetic (hypoglycemic) activity in diabetic rats induced with alloxan (120–150 mg/kg), alleviating symptoms such as fatigue and pain. The efficacy of the medicinal extract (400–500 mg/kg) in treating diabetes in experimental studies is attributed to the presence of flavonoids, which may either promote insulin production or have insulin-like effects.64,65 When administered to both normoglycemic and hyperglycemic rats induced by alloxan at a dose of 400 mg/kg body weight, the alcoholic and aqueous extracts of Anthocephalus cadamba roots demonstrated anti-diabetic effects. Anthocephalus cadamba has exhibited antimicrobial activity against Aspergillus nidulans, Micrococcus luteus, and Escherichia coli. Studies have indicated that A. cadamba extract possesses significant wound-healing potential. Additionally, the aqueous extract of A. cadamba has shown effectiveness against animal foot-and-mouth disease and the causal organism of wheat tundu disease, Rathyibacter tritici.66,67

Figure 5. Anthocephalus cadamba

CONCLUSION

The article suggests that medicinal plants have shown notable efficacy in healing wounds, particularly in individuals with diabetes. Notwithstanding the drawbacks of clinical trials, many people, particularly in underdeveloped nations, persist in using therapeutic plants for treating various ailments and infections, such as

wounds caused by diabetes.68 In one instance, applying an ointment derived from medicinal herbs effectively stopped 85% of diabetic wounds from needing to be amputated. However, the article suggests that Additional investigation and clinical trials are needed to Verify the efficacy, safety, and mechanisms of action of certain therapeutic herbs in the healing of diabetic wounds.69,70

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