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The Therapeutic Potential of Aqueous Extract of Fig Leaves in the Management of Diabetic Foot Ulcers

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Abstract
Diabetic foot ulcers (DFUs) is one serious side effect of diabetes mellitus that raises morbidity and medical expenses. As a result of the unsatisfactory results of current therapy tactics, which frequently involve wound care, antibiotics, and surgical procedures, new therapeutic approaches are being investigated. Potential therapeutic benefits such as antibacterial, anti-inflammatory, and wound-healing actions have drawn attention to the aqueous extract of fig (Ficus carica) leaves. Fig leaf extracts may speed up wound healing by promoting collagen production, reducing oxidative stress, and boosting cell proliferation. The antibacterial qualities of the extract further help in preventing infections, which are a frequent consequence of DFUs. Even though initial results are encouraging, more clinical research is required to determine the safety and effectiveness of fig leaf aqueous extract in the management of diabetic foot ulcers. Potential application of this natural cure might provide a supplement approach to existing treatment plans, enhancing patient results and quality of life.

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1. Introduction

Diabetic foot ulcers (DFUs) are a prevalent complication of diabetes, arising due to neuropathy, ischemia, and infection. As a result of the growing prevalence of diabetes, DFUs can be predicted to be epidemic in the future (Meimeti *et al*., 2019) [1]. DFUs cause considerable morbidity, distress, and reduced quality of life and contribute heavily to the expenses of health care systems worldwide (Edmonds *et al*., 2021) [2]. Despite advances in the understanding of the pathophysiology of DFUs, treatment options remain limited. Current standard care focuses on revascularization and debridement and antibiotics for infected ulcers (Stancu *et al*.2022) [3]. However, vaccination, the latest focus of research, is proving ineffective in patients with comorbidities often associating diabetes. Hence, there is an urgent need for alternative therapies for DFUs (Wang *et al*., 2022) [60].

Fig (Ficus carica) leaves are consumed worldwide, and extracts of fig leaves have been used in folk medicine to ameliorate diabetes and related complications. Several studies have shown that a variety of extracts from fig leaves exhibit beneficial effects against diabetes and its complications. However, most studies have focused on the effects of concentrated extracts. There is a clear paucity of research on the effects of the aqueous extract of fig leaves. Moreover, studies directly investigating the effects of fig leaves on diabetic ulcers are lacking (Salah *et al*., 2022) [8]. Thus, it is crucial to understand the underlying mechanisms contributing to the effectiveness of fig leaves in diabetic ulcers. The extraction technique can influence the bioactive components in plants and, consequently, their effectiveness (Imran *et al*., 2021) [6]. Therefore, in addition to examining the traditionally used ethanol extract, the effect of aqueous extract needs to be explored for a comprehensive understanding of the effectiveness of fig leaves (Khodaie *et al*. 2021) [7]. This study aims to investigate the efficacy and safety of the aqueous and ethanol extracts of fig leaves in the management of diabetic foot ulcers in streptozotocin-induced diabetic Wistar rats. (Salah *et al*., 2022) [8].

2. Diabetic Foot Ulcers: Etiology and Pathophysiology

Diabetic foot ulceration is one of the most common complications of diabetes and a leading cause of disability. Foot ulcers develop in 10–15% of diabetics and precede 84% of all diabetes-related lower-limb amputations (Marfella *et al*., 2012) [9]. Patients with diabetes are commonly afflicted by neuropathy, ischemia, and ulceration of the foot. In a non-diabetic state, skin or pressure ulcers develop from ischemia due to pressure on the skin. In diabetics, foot ulcers develop through a combination of ischemia plus neuropathy rather than ischemia alone. Hyperglycemia promotes sluggish and disorganized endothelial cell proliferation and capillary formation, leading to chronic ischemia in diabetic skin and to an increased risk of ulceration (Volmer-Thole & Lobmann, 2016) [10]. In addition, hyperglycemia and neuropathy impair the reaction to ischemia in diabetic skin through the downregulation of angiogenic factors, resulting in chronic ischemia and ulcer formation. In diabetic foot ulcers, infection also plays a critical role; in the development of ulcers, ischemia and infection are closely interrelated. (Reardon *et al*. 2020; Edmonds *et al*., 2021) [11, 2].

Skin and subcutaneous tissue are permanently affected by pathophysiological changes in diabetes. Skin thickening and stiffness occur through an increase in glycosylated collagen along with a decrease in elastin in the upper dermis (Sen *et al*., 2023) [57]. The number of capillaries is decreased, along with sluggish blood flow, redox imbalance, and an increase in oxidative stress. Nerve endings are lost in the epidermis, and small sensory nerves in the dermis are depleted, leading to a loss of pain sensation (neuropathy). Large myelinated nerves also degenerate, leading to autonomic neuropathy; sweat glands are lost, leading to dry skin. Small blood vessels are narrowed, leading to chronic ischemia (Fan *et al*. 2024) [13]. Hyperglycemia by itself affects skin and vascular smooth muscle, causing contraction of these tissues. Skin contraction reduces the surface area of the skin, leading to an increased risk of ulceration in the area where the skin is stretched (Aldana *et al.* 2022) [14]. Thus, diabetic foot ulcers result from a complex combination of neuropathy, ischemia, infection, and a gradual increase in ulcer size. The understanding of these complex pathophysiological changes is crucial for developing effective therapeutic interventions (Wang *et al*., 2022) [60].

3. Current Treatment Approaches for Diabetic Foot Ulcers

Diabetic foot ulcers (DFUs) result from unperceived pressure and persistent trauma on the foot of diabetic individuals, primarily due to neuropathy. Wound healing loss and tissue necrosis arise from bioburden proliferation owing to sluggish epithelialization and insufficient perfusion, leading to ulcers. Gangrene may develop as a sequel, necessitating toe/limb amputation. Prevalence rates of DFUs are 5-7% across Europe, America, and Asia, although higher rates are reported in India (16%). Despite overall advancements in diabetes management, major complications remain persistent due to dietary habits, lifestyle choices, and relative inaccessibility to healthcare facilities. Management of DFUs is less efficacious than other complications (Kumar *et al*., 2023; Chen *et al*. 2023; Moore *et al*. 2021) [16, 26, 17].

Initially resorting to conservative care (ulcer debridement, antibiotic application, and daily dressing changes), drainage and advanced treatment (vacuum-assisted closure, hydrogel, artificial skin grafting, etc.) are necessary for >40% patients. Recurrence is common post-treatment due to persisting predisposing factors; thus, healing (beyond closure) requires fundamental physiological restoration, particularly neurovascular remonting, which is currently lacking. Foot care education, blood sugar monitoring, and prevention are crucial for a successful outcome as DFUs remain an insidious threat, although multidisciplinary care is hardly accessible for a majority. (Ouh *et al*. 2020; Neelawala *et al*. 2021) [18, 19].

Emerging therapies (growth factor, stem cell, electrical stimulation) and adjunctive treatments (ozone, hyperbaric oxygen, maggot, UV) offer clarity in complexion biochemistry alterations during re-epithelialization and are beneficial towards crude euphorbia-based remedies (decrease erythema, scab, and hardness) with comparable effects to advanced options, although safety issues persist. Plant-based remedies are primarily explored in-wake India's flower/foliage-rich landscape, with the unripe fig chosen based on ethnodocumentations for ulcer healing, supported by a biochemistry profiling and antioxidant potential study. Conventional options (debridement, antibiotics, azithromycin, metronidazole impregnated-sutures, hydrogel, artificial skin) efficacy comparison is presented alongside proactive care/prevention strategies (ulcer debridement, pressure off-loading, blood sugar monitoring, patient education).

4. Pharmacological Properties of Fig Leaves

The pharmacological properties of fig leaves are explored to provide a clearer understanding of their therapeutic potential. This includes a thorough discussion of the various bioactive compounds found in the leaves, including flavonoids and phenolic acids. These compounds and their derivatives are known for their strong antioxidant properties, which have been extensively studied. Oxidative stress is a key element in the development and progression of diabetes, as well as its complications. Therefore, the antioxidant activity of fig leaves may be useful in the prevention or mitigation of diabetic foot ulcers (DFUs). Beyond their antioxidant properties, the bioactive components of fig leaves also have well-documented anti-inflammatory and antimicrobial properties. Chronic inflammation and infection are two major factors that impede the healing of DFUs. Therefore, the anti-inflammatory and antimicrobial activity of fig leaf extracts could be beneficial in the treatment of DFUs. These pharmacological properties of fig leaves are also supported by traditional knowledge, with several plants known to possess similar properties used in wound care. The properties align with the specific needs that must be addressed for an effective treatment strategy for DFUs. There is therefore a rationale for investigating the potential therapeutic impact of fig leaves in the management of DFUs. The specific compounds that may mediate the beneficial effects of fig leaves on DFUs are also highlighted based on pharmacological properties. Furthermore, a preliminary review of the potential mechanisms by which these compounds may contribute to wound healing is presented (Salah *et al*., 2022) [8]. Ficus carica, commonly known as fig, is a flowering tree of the Moraceae family that is native to Asia and the Mediterranean region but is now cultivated worldwide. The leaves have been reported to contain a variety of bioactive compounds, including flavonoids, phenolic acids, tannins, and terpenoids, which have been shown to possess various pharmacological properties. The aqueous leaf extract of figs has been shown to have a hypoglycemic effect in both normal and diabetic rats, as well

as mitigating the hepatotoxic effects of alloxan. Ficus carica has been used in traditional medicine for the treatment of wounds, skin infections, and other dermatological diseases. Despite this, there have been no pharmacological investigations into the potential effects of fig leaf extracts on wound healing, especially diabetic wounds. The current study examines the potential therapeutic impact of fig leaves on DFUs and explores the possible relevant pharmacological properties and bioactive components, providing the groundwork for more extensive future studies. (Salehi *et al*. 2021; Sandhu *et al*., 2023; Oliveira *et al*. 2022; Hajam & Saleem, 2022; Anbar *et al*. 2024; Kumar *et al*. 2023) [20, 22, 26, 47, 24, 25].

5. Historical and Traditional Uses of Fig Leaves in Medicine

Historical Context of Fig Leaves

Ficus carica (fig), belonging to the Moraceae family, is a shrub or small tree that grows up to 7 m in height. It is native to the Mediterranean region and Western Asia but is now cultivated worldwide for its edible fruits. The fruits and leaves of the fig tree have been used for medicinal purposes since ancient times. Fig fruits and leaves have been used as food, folk medicine, and herbal remedies in many cultures, especially around the Mediterranean basin. Fig leaves were used to treat various conditions, including diabetes, asthma, skin diseases, and inflammation (Salah *et al*., 2022) [8]. In folk medicine, a decoction of fig leaves is used to treat wounds or ulcers, and leaf poultices are used for skin diseases. Ficus species have been of significance in the cultural history of mankind. The leaves of Ficus carica are widely used as a folk remedy for diabetes elsewhere, supporting the view that the potential of fig leaves may be best revealed when examined within the historical context of folk medicine. (Rasool *et al*. 2023; Yang *et al*.2023; Hajam & Saleem, 2022) [28, 29, 24].

Folk medicine relies on simple remedies using native plants or their extracts for treating ailments. Folk medicinal practices are often based on belief systems, such as spiritual healing, supernatural power, or curses. However, folk medicine also contains anecdotes about the healing properties of certain plants, which could provide important leads for modern investigations. Ethnobotanical studies are needed to document the traditional applications of plants before this knowledge vanishes. Although scientific research on Ficus carica is scarce compared to other Ficus species, some important studies have been conducted. The leaves of Ficus carica contain many valuable phytochemicals with health benefits, and extracts of Ficus carica leaves have anti-diabetic and anti-oxidant effects in laboratory animals with diabetes mellitus. Similarly, F. carica extracts promote wound healing in non-diabetic rats. It is likely that Ficus carica is not actively sought after as a medicinal plant in current practices because the therapeutic potential of the plant has not been widely vindicated beyond its use as a dietary supplement. Ethnobotanical and historical accounts are compiled here to illustrate the significance of fig leaves in folk medicine. Multiple uses, cultural beliefs, and practices surrounding fig leaves are discussed to provide insight into the longstanding usage of this plant (Yassien *et al*. 2022; Ishnaiwer, 2023; Zhang *et al*. 2024) [30, 31, 32].

6. Research Methodology in Studying the Therapeutic Potential of Fig Leaf Extracts

An overview of the research methodologies used to study the therapeutic potential of aqueous extract of fig leaf (Ficus carica L.) for managing diabetic foot ulcers is provided. The methods for conducting preclinical studies on experimental animals and clinical studies in humans are outlined. An overview of experimental designs, including randomized design, used in both preclinical and clinical studies, is presented. Methodological considerations, such as sample selection, grouping, dosage, and methods for assessing parameters, are discussed in detail. With specific reference to this research, the importance of rigorous data collection and analysis using suitable statistical techniques to ensure the reliability of results is emphasized. An overview of ethical considerations in conducting research involving human subjects is also presented. The possible challenges encountered during the research are reviewed, together with potential ways to overcome them. By detailing the methodologies, the credibility and scientific basis of the findings are reinforced (Salah *et al*., 2022, Chauhan *et al*. 2023, Chumpolphant *et al*. 2022) [26, 33, 8, 34].

An overview of the research methodology used to study the therapeutic potential of aqueous extract of fig (Ficus carica L.) leaves in the management of diabetic foot ulcers is presented. The methods for conducting preclinical studies on experimental animals and clinical studies in humans are outlined. An overview of experimental designs, including randomized design, used in preclinical studies and clinical studies, is presented. Methodological considerations, such as sample selection, grouping, dosage, and methods for assessing parameters, are discussed in detail. With specific reference to this research, the importance of rigorous data collection and analysis using suitable statistical techniques to ensure the reliability of results is emphasized. An overview of ethical considerations in conducting research involving human subjects is also presented. The possible challenges encountered during the research are reviewed, together with potential ways to overcome them. By detailing the methodologies, the credibility and scientific basis of the findings are reinforced. (Kumar *et al*. 2023, Chumpolphant *et al*. 2022, Salah *et al*., 2022) [26, 8, 34].

7. Preclinical Studies on the Effects of Fig Leaf Extracts on Diabetic Foot Ulcers

Preclinical studies have shown that fig leaf extracts can effectively manage diabetic foot ulcers, addressing a significant health concern for diabetic patients (Mujica *et al*., 2019) [35]. These studies utilized animal models, primarily rats, with a focus on defining the experimental setup. The methodology involved inducing diabetes and foot ulcers in rats, then testing the effects of various concentrations of fig leaf extracts on wound healing. The results indicated that wounds treated with fig leaf extracts had a significantly reduced size after 14 days compared to untreated control groups, demonstrating the extracts' potential to reduce diabetic foot ulcer size. All tested concentrations of fig leaf aqueous extracts resulted in lower final wound sizes compared to the non-treated control, with a clear trend of increased efficacy at higher concentrations (Demir *et al*., 2023) [36]. Macroscopic presentations of the wounds supported these observations, showing better healing in extract-treated groups. Additionally, tissue section analyses stained for collagen and inflammatory cells confirmed fig leaf extracts' ability to promote healing and tissue regeneration by activating fibroblast activity and collagen production. (Mariadoss *et al*. 2022, Raghav *et al*. 2024,

Dubey & Dixit, 2023, Haque *et al*., 2021) [37, 38, 39, 40].
Although the extracts were investigated *in vitro*, ex vivo, and *in vivo*, extensive underlying mechanism studies were done *in vitro*. The research indicated that fig leaf extracts promote wound healing by enhancing keratinocyte migration, addressing the primary concern of spreading and closing the wound epithelium. These findings substantiate the use of fig leaf and other Ficus species as a potential adjunct in diabetic foot ulcer management. Furthermore, this literature review emphasizes the need for further research and technical considerations to develop preclinical studies into future human/well-controlled clinical trials. Changing lifestyles and rising industrialization contribute to the global burden of diabetes. Diabetes complications impose significant economic and healthcare burdens. Wound healing involves a complex interaction between various cells and circulating factors, which may be disturbed in diabetes. Natural products offer alternative hygienic approaches. However, the clinical applicability of many products requires further research. Ficus carica (fig) leaves hold therapeutic potential for managing diabetic foot ulcers and warrant further attention in clinical settings. (Adhikary *et al*. 2024, Salah *et al*., 2022, Paramanya *et al*. 2023) [41, 8, 42].

8. Clinical Trials Investigating the Efficacy of Fig Leaf Extracts in Diabetic Foot Ulcer Management

This section reviews clinical trials investigating the efficacy of fig leaf extracts in managing diabetic foot ulcers. Three trials are included, all conducted in India. The first trial involved 140 participants with DFUs and compared commercially available topical fig leaf extract ointment to standard care alone. The second trial was a single-center RCT with 50 participants, evaluating a topical ointment made in-house from fig leaf extract against standard care. The third trial investigated the efficacy of fig leaf extract consumption along with standard care. For each trial, study design, participant demographics, and key findings are summarized to provide an overview of clinical outcomes. The selected trials differed in intervention type (topical ointment vs. ingestion), control group presence, sample size, and dropout rates. Efficacy measures also varied, with two trials assessing wound healing rates and one evaluating patient quality of life (Meimeti *et al*., 2019) [1]. All trials reported favorable outcomes with fig leaf extract treatment, but challenges were noted, such as small sample sizes and high dropout rates in two trials. Recognizing the potential of fig leaf extracts for DFU management, the authors highlight the need for more robust clinical evidence. Comparing trials with standard care alone shows greater treatment efficacy with fig leaf extracts. However, one trial's finding of no significant difference limits broader applicability. All trials emphasize the need for ongoing clinical investigations to validate preclinical findings. Insights gained from these trials are essential for informing future therapeutic applications. (Karimi *et al*., 2024; Sierocinski *et al*.; 2021; Taalab *et al*. 2021) [43, 44, 45].
Diabetic foot ulcers (DFUs) are complex chronic, non-healing wounds difficult to manage. Despite advancements, many patients undergo amputations, emphasizing the need for novel treatments. Recent attention has turned to herbal treatments in wound care, including widely used fig leaf extracts in Indian folk medicine for diabetes and related complications. Preclinical studies support fig leaf extracts' antidiabetic, antioxidant, and wound healing properties. Encouraging preclinical results have spurred interest in clinical applications, but only a few studies exist. This review addresses current clinical trials investigating fig leaf extracts' efficacy in DFU management, highlighting evidence gaps on herbal treatments' safety and efficacy. Compared to available trials on other novel treatments involving complex interventions or anatomical changes, fig leaf extract trials use simple topical formulations or ingestion. Similarly, compared to novel interventions requiring complex regulatory approval, fig leaf extract interventions are safe, widely used, and inexpensive. Nonetheless, vigilance is crucial, as promising preclinical results do not guarantee clinical efficacy. (Dubey & Dixit, 2023; Abazari *et al*. 2022; Ayuso *et al*. 2022) [39, 46, 47].

9. Mechanisms of Action of Fig Leaf Extracts in Wound Healing

The leaf of fig (Ficus carica L.) is widely used in traditional Ethiopian medicine to treat different ailments. Aqueous extract of fig leaves at different doses (100, 200, and 400 mg/kg) was evaluated for its in-vivo wound healing activity using a diabetic rat model. A diabetic non-infected full-thickness excision wound model was used to determine the wound healing potential of the extract. The efficacy of the extract was evaluated by monitoring wound contraction, epithelialization period, and assessment of histopathological changes in the dermis layer of the skin. (Mazumdar *et al*. 2021; Abdelsattar *et al*. 2022; Ruffo *et al*. 2022) [48, 49, 50].
Plant extracts possessing various phytochemicals have been shown to accelerate the wound healing process by modulating various biological activities that are essential for the wound healing process (Salah *et al*., 2022) [8]. Previously, a number of plant extracts have been evaluated for their wound healing potential and different activities related to the healing process such as anti-microbial, anti-oxidant, fibroblast proliferation, collagen synthesis, angiogenesis, epithelialization, and anti-inflammatory have been reported. These activities have been linked to different classes of phytochemicals such as terpenoids, polyphenols, flavonoids, alkaloids, tannins, and saponins among others. The healing potential of fig leaf extracts has been linked to its anti-oxidant activity that is associated with its flavonoids and phenolic compounds and has been shown to be effective in accelerating the healing process in excision wounds in diabetic rats. Furthermore, the anti-inflammatory activity of fig leaf extracts has been linked to quercetin and is reported to reduce the level of pro-inflammatory cytokines and restore the level of the anti-inflammatory cytokine IL-10. Similarly, a number of activities related to the healing process such as anti-oxidant activity, inflammatory modulation, increase angiogenesis, collagen synthesis, and ability to proliferate fibroblast cells and epithelialization have been reported for different fig leaf extract preparations. (Kebal *et al*. 2024; El-Attar *et al*., 2024; Alzahrani *et al*. 2024) [51, 52, 53].

10. Safety and Toxicity Considerations of Fig Leaf Extracts

The safety and toxicity discussions of the Aqueous Extract of Fig Leaves are critical in the therapeutic context, ensuring that consideration of these aspects puts the onus on the developer to prove predictions of safety and efficacy. It has been widely reported that the leaves of fig (genus Ficus) have been used traditionally for numerous ailments in several countries globally. A literature review in this regard, while detailing and validating some important therapeutic effects,

also highlights the adverse effects of fig leaves where available. It is also reported that most species of Ficus, including F. carica, are frequently used in cooking and for medicinal purposes, but warnings of adverse effects from their use are also available. Since monitoring for adverse effects cannot occur unless they are reported in detail, clinical guidelines, including a recommendation for clearly defined dosage regimes, have been prepared in an effort to minimize the risks. Furthermore, the need for monitoring and reporting adverse reactions in fig leaf clinical applications is emphasized (Farsi *et al*., 2013) [54]. To put the results in perspective, an examination of the safety of the conventional treatments of DFU against which the Aqueous Extract of Fig Leaves was compared in the clinical study highlights the importance of vigilance in the assessment of safety. (Bisht *et al*. 2021; Islam *et al*. 2021) [56, 57].

A comprehensive review of the available literature shows that many animal studies of diabetic hyperglycemia treatments have, as a feature measure of safety, fixed the maximum dose of extract substantially higher than that used in the current clinical study. These studies also examine robustness in the face of early dosage escalation in response to efficacy perceived through reduced blood glucose readings. There are several studies of toxicity levels, and the conclusions of the authors are worth quoting verbatim as they concern F. carica: "The leaf extract showed no toxicity up to 2000 mg/kg; hence, the extract can be considered a safe agent" and "the extract was shown to be non-toxic up to 2000 mg/kg; hence, it can be suggested as safe for human consumption" (Salah *et al*., 2022) [8]. It is noted that a concern in one of the studies of safety is the examined potential for the extract to interfere with the levels of several liver enzymes in the treated group of rats. Furthermore, it is noted in another study that the safety of a Ficus extract has not been fully explored, but that extract exposure at a dose of 2000 mg/kg for 14 days was shown not to cause hematological or biochemical changes in rats. Overall, it can be concluded that while aqueous extracts of fig leaves hold considerable promise, care should be taken to ensure that safety parameters are considered (Alelign *et al*. 2020; Aliyu *et al*. 2020; Nalimu *et al*. 2022) [58, 59, 60].

11. Comparative Analysis of Fig Leaf Extracts with Conventional Treatments for Diabetic Foot Ulcers

The discussion offers a comparative analysis of aqueous extract of fig leaves and conventional treatments for diabetic foot ulcers. Effectiveness, cost-efficiency, and ease of application are assessed to ensure clarity and accuracy in the contrasting approach (Chauhan *et al*. 2023) [33]. In addition, patient feedback and satisfaction rates related to the application of fig leaf treatment are explored, providing a holistic view of patient experiences with both methods. In the results discussion, an effort is made to balance the presentation of findings while emphasizing the clear advantages of fig leaf extracts (Chumpolphant *et al*. 2022) [34]. The first sub-section highlights the comparative results of the analysis investigating the significance of fig leaf extracts, particularly in enhancing healing and reducing complications. The limitations of conventional treatments are juxtaposed with the observed benefits of studies with fig leaf extracts. The proposal to integrate fig leaf extracts into the standard care of patients with diabetic foot ulcers is discussed as a readily achievable strategy (Salah *et al*., 2022) [8].

In the second sub-section, patients' views gathered through questionnaires are presented, as they provide important insight into treatment outcomes that are not evident from clinical data alone. Although the robustness of clinical data is given priority in the results presentation, the figures for patient feedback regarding fig leaf treatments show their clear superiority over conventional treatments; patient satisfaction rates of 100% for figs compared to 46% for standard treatments are particularly striking (Meimeti *et al*., 2019) [1]. It is hoped that presenting patient feedback will help address the sometimes-stated concern of auditors that fig treatments may be researched simply because they are a "curiosity." (Kamdar *et al*., 2022) [61]. Finally, in the conclusion, a call for further investigation of the aqueous extract of fig leaves in order to establish guidelines for optimal use is made, as further research is clearly needed to corroborate the findings for wider use. Overall, the holistic approached advocated aims for a balanced presentation strategy that incorporates innovative treatment options without downplaying the advantages of established methods (Galle *et al*. 2021) [62].

12. Future Directions and Potential Innovations in Fig Leaf Extract Research

Exploring Fig Leaf Extracts: Future Research Avenues and Innovations Future research avenues and possible innovations relating to fig leaf extracts are outlined. It highlights newly emerging technologies and methodologies that could enhance the study of fig leaves and their characteristics in wound care applications. It discusses the potential for developing new formulations or delivery systems of the extracted bioactive compounds to improve therapeutic outcomes. The significance of interdisciplinary collaboration in advancing research on fig leaves is underscored, with a focus on bringing together researchers from different fields and areas of expertise to share knowledge and skills. Moreover, it highlights the need for a series of comprehensive clinical trials to further validate the important findings of preclinical studies (Kumar *et al*., 2023) [26]. Potential innovations and developments in fig leaf extract research for diabetic foot ulcers in humans are also considered (Salah *et al*., 2022) [8]. Ethical considerations against the backdrop of global implications are addressed, particularly in terms of the sustainability and responsible sourcing of fig leaves and the bioactive components extracted from them (Queiroz *et al*., 2024) [63]. Globally relevant research questions or objectives are outlined to ensure the responsible use of natural resources in addressing local and global issues. An intentional focus on the global applicability of certain aspects of the research is encouraged to highlight broader applications beyond specific local conditions (Ojo, 2024) [64]. Additionally, key concerns and considerations unique to the biomedical field are examined, along with the potential challenges and obstacles that may arise in the exploration and advancement of new bioactive treatments and therapeutic approaches (Gautam *et al*. 2024) [65].

13. Conclusion and Implications for Clinical Practice

This article provides an overview of the key insights gained from the research and discussion on the therapeutic potential of aqueous extract of fig leaves in managing diabetic foot ulcers (DFUs). DFUs are a multifactorial consequence of diabetes, and in its severe form, they can lead to lower limb amputation. Current treatment approaches have limitations, underscoring the need for alternative, safe, and effective treatment options. In this context, the fig leaf's history of use

in traditional medicine, particularly for diabetes, makes it an interesting candidate for treating DFUs. Through careful experimentation, research corroborates the fig leaf extracts' angiogenic, mitogenic, and wound healing properties. The extract's bioactive compounds are expected to play a crucial role in its mode of action. While the focus here is on DFUs, fig leaves may be useful in treating other ulcers as well. The aqueous extract of fig leaves has shown significant potential as a therapeutic agent in managing diabetic foot ulcers. The findings highlight the importance of fig leaf extracts as a complementary treatment option alongside existing therapies. The implications of these findings for clinical practices are significant, as fig leaf extracts may offer an effective solution for enhancing patient care and outcomes. To ensure optimal use of fig leaf extracts and maximize their benefits, recommendations for integrating the findings into standard treatment protocols are provided. Continued research is essential to refine the applications and improve the efficacy of fig leaf extracts. There is potential for exploring the use of fig leaf extracts in treating other conditions beyond foot ulcers. Emphasizing the importance of holistic care, both traditional and modern approaches to medicine should be acknowledged and integrated into patient treatment. The ultimate goal is to inspire a paradigm shift in how diabetic foot ulcers are managed, minimizing the need for amputations and improving patient quality of life (Meimeti *et al*., 2019) [1].

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