



Review Article

Antidiabetic Activity of *Catharsntus Pusillus*: A Review

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Abstract:

There are over 800 species of ficus, an evergreen tree in the Moraceae family. The entire plant, particularly the leaves of *Ficus religiosa* and *Ficus benghalensis*, has long been thought to aid in the healing of wounds. Additionally, the plant's leaves are said to possess antibacterial, antioxidant, and anti-inflammatory qualities. This study assessed the ability of aqueous extracts of *Ficus religiosa* and *Ficus benghalensis* to heal wounds in rats by estimating biochemical parameters and utilizing the excision, incision, and dead space models. The breaking strength and the percentage of wound contraction or closure were assessed in the incision and excision wound models, respectively. The effectiveness of medications against the proliferative and remodeling phases of wound healing was assessed in the dead space model. In addition, GSH, Catalase and MDA estimation studies were employed to assess the efficacy of both the plants in vivo. The treatment of wound with ointment containing aqueous extracts of *Ficus religiosa* and *Ficus benghalensis* exhibited significant wound healing. The results were comparable to standard drug povidone iodine ointment, in terms of wound contraction, tensile strength and histopathological parameters. A significant antioxidant activity was observed as evidenced from decreased level of MDA and increased the level of GSH, catalase in extract treated animals as compared to control animals.

Keywords: Ficus Religiosa, Remodeling, Biochemical, Catalase, MDA, GSH

Introduction

Wounds are a type of injury that can cause the skin or other bodily tissues to break, and they can be caused by accidents, surgery, stitches, or surgical trauma, as well as several medical diseases. Minor wounds are generally not dangerous, but they should be cleaned. Serious and infected wounds may require immediate

medical attention, followed by a visit to your doctor. Seek medical assistance if the cut is deep, cannot be closed, cannot be stopped from bleeding, has dirt that can't be removed, or doesn't heal. Wound healing is a dynamic and intricately regulated physiological process involving multiple stages. It begins with

hemostasis to stop bleeding and progresses through inflammation, proliferation, and remodeling phases. Inflammation clears debris and defends against infection, while proliferation involves angiogenesis, collagen synthesis, and epithelialization to rebuild damaged tissues. Wound remodeling ensures tissue strength and durability. Proper wound care, including cleanliness, protection, and infection control, is crucial. Factors influencing wound healing encompass nutrition, blood supply, wound size, and comorbidities. Healthcare professionals play a pivotal role in evaluating wounds and recommending treatments to optimize healing. Understanding the stages and factors involved in wound healing is essential for effective management and patient recovery. Wound may be defined as a loss or breaking of cellular and anatomic or functional continuity of living tissue. The prevalence of chronic wounds in the community was reported as 4.5 per 1000 population where as that of acute wounds was nearly doubled at 10.5 per 1000 population. It is an often encountered problem in clinical practice. Wound healing refers to the body's natural process of restoration of tissue architecture and function after an injury. It involves inflammation, cell proliferation, and contraction of collagen lattice formation (Reddy, 2008). On the basis of etiology, wounds can be broadly categorized into acute or chronic form including surgical wounds, traumatic wounds, lacerations, burns, etc. Plants have been used for the treatment of various ailments of skin and dermatological disorders especially cut, wounds, burns from the ancient time (Kumar, 2007). Moreover, it has been estimated that 80% of the population of developing countries is unable to afford pharmaceutical drugs and rely on traditional herbal medicines.

These compounds possess potent antioxidant properties that help prevent a number of diseases linked to oxidative stress, including dyslipidemia, diabetes, and atherosclerosis. Since ancient times, it has been widely used to treat a wide range of illnesses. For example, swarsh (leaf juice) has been used to treat scabies, cough, asthma, sexual disorders, hematuria, pain

in the teeth and ears, headache, eye problems, and gastric problems. Leaf decoction has been used as an analgesic for toothaches, and stem bark has been used to treat gonorrhoea, bleeding, diabetes, diarrhoea, fractures, antiseptic, and astringent, among other conditions.

Numerous substances, such as growth factors, cytokines, and extracellular matrix components, are involved in the healing of wounds. Epidermal Growth Factor (EGF) is one of several growth factors that promotes overall wound healing by promoting angiogenesis, collagen production, and cell growth. Platelet-derived growth factor (PDGF) promotes the formation of new tissues by promoting angiogenesis, collagen synthesis, and cell division. The regulation of cell proliferation, differentiation, and extracellular matrix production by Transforming Growth Factor-beta (TGF- β) affects the closure of wounds. Certain cytokines, such as interleukins, regulate inflammation and immune responses, primarily impacting immune cell activity and tissue repair mechanisms. Collagen and other extracellular matrix constituents support cell migration and offer structural integrity, which promotes wound healing and tissue regeneration. Fibronectin facilitates tissue repair by encouraging cell migration and adhesion.

Many medicinal plants have been explored to exhibit wound healing properties at an extensive rate from the traditional period. These plants generally exhibit many bioactive components for antioxidant properties and finally contribute to therapeutic effectiveness for wound healing agents. These bioactive Compounds can be broadly categorized into the following criteria:

These antioxidants possess anti-inflammatory properties that may reduce inflammation at the wound site, creating a favorable environment for healing. Phenolics could stimulate collagen synthesis and enhance tissue regeneration, contributing to wound closure.

Peepal, or *Ficus Religiosa*, is widely used in traditional medical systems such as Ayurveda, Unani, and Siddha in a variety of formulations.

All of the *F. religiosa*'s parts show a broad range of therapeutic value as anthelmintic, antiulcer, antiasthmatic, anticancer, antioxidant, antidiabetic, antimicrobial, and anticonvulsant agents. *Ficus religiosa* has long been used in folk medicine to treat a variety of conditions, including scabies, asthma, cough, sexual dysfunction, diarrhea, haematuria, migraines, eye issues, stomach issues, and respiratory and respiratory disorders. The infusion of leaves has analgesic properties that relieve toothaches. The stem bark of the peepal tree is used as an antiseptic, astringent, and antidote for treating gonorrhoea, bleeding, paralysis, diabetes, ulcers, and a variety of skin conditions. Bark phytosterols are used as an effective stimulant of the central nervous system. Fruit is laxative and digestive (4-5). The current study envisages evaluating wound healing effect employed in animal models due presence of flavonoids , polyphenolic compound and antioxidants activity. *Ficus religiosa*, commonly known as the sacred fig or peepal tree, is a species of fig tree that holds cultural and religious significance in various parts of the world, particularly in Hinduism, Buddhism, and Jainism. The potential role of *Ficus religiosa* in wound healing is primarily based on its traditional use in some cultures and anecdotal evidence. *Ficus religiosa* contains compounds with antioxidant properties, such as flavonoids and polyphenols. Antioxidants can help protect cells and tissues from oxidative damage, which is important in the context of wound healing. Inflammation is a key part of the body's natural response to injury, but excessive or prolonged inflammation can hinder the healing process. Some components of *Ficus religiosa* may have anti-inflammatory properties, potentially aiding in the regulation of the inflammatory phase of wound healing. In some traditional systems of medicine, *Ficus religiosa* has been used for its potential antimicrobial properties. Preventing or treating infections in wounds is crucial for successful healing. Collagen is a critical protein involved in wound healing, as it provides structural support to the repaired tissue. Some compounds in *Ficus religiosa* may stimulate collagen synthesis. It's

important to note that while *Ficus religiosa* may have these potential properties, scientific research on its wound healing effects is limited, and it should not be considered a substitute for standard wound care practices.

Ficus Religiosa:

Ficus religiosa, commonly known as the Sacred Fig or Bo Tree, is a species of fig tree considered sacred in various cultures. Here's a general overview of the microscopic, macroscopic, physiological aspects, as well as the collection and extraction processes for *Ficus religiosa*:

Microscopic Analysis:

1. Leaf Structure:
 - Examine the cellular structure of the leaves, including the epidermis, stomata, and vascular bundles.
 - Identify any specialized structures such as trichomes or latex vessels.

Macroscopic Analysis:

1. Overall Plant Characteristics:
 - Observe the general appearance of the tree, considering its size, shape, bark, and growth habits.
 - Note the characteristics of leaves, including their shape and arrangement.
2. Fruit Characteristics:
 - Study the structure and appearance of the figs produced by *Ficus religiosa*.

Physiological Analysis:

1. Metabolic Pathways:
 - Explore biochemical pathways, especially those related to the synthesis of secondary metabolites that may have medicinal properties.
2. Adaptations to Environment:
 - Understand how *Ficus religiosa* adapts to its environment, including resistance to pests and diseases.

Collection of Plant:

1. Selection:
 - Ensure accurate identification of *Ficus religiosa*.
 - Choose healthy specimens for collection.

2. Timing:
 - Harvest leaves, bark, or other plant parts at the appropriate time in the growth cycle.
3. Parts Collected:
 - Depending on the intended use, collect relevant plant parts, which may include leaves, bark, or aerial roots.

Extraction Process:

1. Harvesting:
 - Clean the collected plant material to remove any foreign matter.
2. Drying:
 - Dry the plant material to reduce moisture content and prevent microbial growth.
3. Extraction Methods:
 - Solvent Extraction: Use suitable solvents (e.g., ethanol) to extract bioactive compounds from the dried plant material.
 - Water Extraction: For certain compounds that are water-soluble.
4. Concentration and Purification:
 - Concentrate the extract by removing excess solvent or water.
 - Purify the extract if necessary, using techniques such as chromatography.
5. Analysis:
 - Conduct chemical analysis to identify and quantify the compounds present.
 - Ensure quality control measures are implemented.



Ficus Religiosa

The leaf juice has historically been used to treat a variety of conditions, including scabies, asthma, cough, diarrhea, haematuria, migraines, eye issues, stomach issues, and respiratory and sexual disorders. The leaf infusion was applied to treat toothaches. The fruits were used to treat scabies, respiratory conditions like asthma, and other conditions. The stem bark was used as an antiseptic, astringent, and antidote for gonorrhea, bleeding, paralysis, diabetes, diarrhea, and bone fractures. Physical and chemical characteristics: Ficus religiosa fruit powder's physical and chemical analysis revealed the following: 8.99% loss on drying, 5.88% total ash, 0.60 percent acid-insoluble ash, 33.10% water soluble, and 28.80% alcohol soluble extractive. Chemical components: The plant was found to contain sugars, alkaloids, terpenoids, flavonoids, glycosides, tannins, phenols, saponins, and steroids, according to a preliminary phytochemical analysis. The total phenol content present in one milligram of aqueous and ethanolic extracts of the bark was 497.77 and 375.23 μ g, respectively.

The aqueous extract of bark of Ficus religiosa was investigated for its anti-inflammatory effect and for its protective effect on mast cells against degranulation. A significant anti-inflammatory effect was observed in both acute and chronic models of inflammation. The extract also protected mast cells from degranulation induced by various degranulations. The effect of a methanol extract of Ficus religiosa leaf was studied in lipopolysaccharide (LPS)-induced production of NO and proinflammatory cytokines, such as tumor necrosis factor-alpha (TNF-alpha), interleukin-beta (IL-1beta) and IL-6 in BV-2 cells, a mouse microglial line. Methanol extract of Ficus religiosa leaf inhibited LPS-induced production of NO and proinflammatory cytokines in a dose-dependent manner. Methanol extract of Ficus religiosa leaf also attenuated the expression of mRNA and proteins of inducible nitric oxide synthase (iNOS) and proinflammatory cytokines. The molecular mechanism of methanol extract of Ficus religiosa leaf-mediated attenuation included down-regulation of the extracellular

signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (MAPK) signaling pathway, and suppression of the nuclear factor kappaB (NF-kappaB) activation. Different fractions of dried leaves of *Ficus religiosa* were evaluated for analgesic and anti-inflammatory activity using different models of pain and inflammation.

The ointment form (5 and 10%) of *Ficus religiosa* extracts was tested for its ability to promote wound healing in Wistar albino rats using incision and excision wound models. In every wound model examined, ointments containing 5 and 10% extracts from the roots of *Ficus religiosa* greatly increased the rate of wound healing. They accelerated the rate at which wounds contracted, shortened the time it took for the epithelium to grow, strengthened the skin, and raised the amount of hydroxyproline. Using excision and incision wound models, the wound healing efficacy of *Ficus religiosa* hydroalcoholic leaf extract ointment (5 and 10%) was investigated in rats. The rate of wound contraction, the length of the epithelialization phase, and the skin-breaking strength were used to gauge how well the wound healed. In both wound models, the wound-healing activity was significantly enhanced by both (5% and 10% ointments).

Conclusion: The present review about the various formulations, it might be helpful to read the current Ashvattha review. Numerous studies on animals suggest that *Ficus religiosa* may have anti-inflammatory, hypoglycemic, hypolipidemic, antioxidant, and immunomodulatory effects. Ashvattha is said to possess properties of Seet, Ruksha, Guru, and Kashya in various Ayurvedic texts. In this manner, Ashvattha can be used to treat a variety of illnesses.

References

1. Rubin, Robert J. (1999) The economic impact of *Staphylococcus aureus* infections in New York city hospitals. *Emerging Infectious Diseases* 1999; 5: 9-17.
2. Stewart PS, Costerton JW. (2001) Antibiotic

- resistance of bacteria in biofilms. *Lancet* 2001; 358(9276):135-8.
3. R. M. Donlan, (2001) "Biofilm formation: a clinically relevant microbiological process," *Clinical Infectious Diseases*, vol. 33, no. 8, pp. 1387–1392, 2001.
4. Vishnu Sharma, Sweta Mishra et al. (2019) A Review on *Ficus religiosa* (Sacred Fig). *International Journal of Research and Analytical Reviews* 2019;6(2): 901-906.
5. Ulak G, et al. (2018) Neuronal NOS inhibitor 1-(2- trifluoromethylphenyl)-imidazole augment the effects of antidepressants acting via serotonergic system in the forced swimming test in rats.
6. Ulusoy S, et al, (2023) Analysis of wound types and wound care methods after the 2023 Kahramanmaraş earthquake. *Jt Dis Relat Surg.* 2023 May 18;34(2):488-496.
7. Flynn K, et al, (2023) Chronic Wound Healing Models. *ACS Pharmacol Transl Sci.* 2023 Apr 19;6(5):783-801.
8. Ozgok Kangal et al, (2023) Wound Healing. 2023 May 1. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. PMID: 30571027.
9. T Ashwini, et al, (2023) Transforming Wound Management: Nanomaterials and Their Clinical Impact. *Pharmaceutics.* 2023 May 22;15(5):1560.
10. Derwin R, et al, (2023) Wound pH and temperature as predictors of healing: an observational study. *J Wound Care.* 2023 May 2;32(5):302-310.
11. Wallace HA, et al, (2023) Wound Healing Phases. 2023 Jun 12. In: *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. PMID: 29262065.
12. Burhan A, Khusein NBA, Sebayang SM. (2022) Effectiveness of negative pressure wound therapy on chronic wound healing: A systematic review and meta-analysis. *Belitung Nurs J.* 2022 Dec 27;8(6):470-480.
13. Bayat M, Albright R, Hamblin MR, Chien S. (2022) Impact of Blue Light Therapy on Wound Healing in Preclinical and Clinical Subjects: A Systematic Review. *J Lasers Med Sci.* 2022 Dec 17;13:e69.

14. Ongarora BG. (2022) Recent technological advances in the management of chronic wounds: A literature review. *Health Sci Rep.* 2022 May 19;5(3):e641. doi: 10.1002/hsr2.641.
15. Kolimi P, et al, (2022) Innovative Treatment Strategies to Accelerate Wound Healing: Trajectory and Recent Advancements. *Cells.* 2022 Aug 6;11(15):2439.
16. Sitohang NA, et al, (2022) Acceleration of wound healing by topical application of gel formulation of *Barringtonia racemosa* (L.) Spreng kernel extract. *F1000Res.* 2022 Feb 15;11:191.
17. Monika P, et al., (2022) Challenges in Healing Wound: Role of Complementary and Alternative Medicine. *Front Nutr.* 2022 Jan 20;8:791899.
18. Madiwalar MB, Pradeep S S, Hiremath RR, Killedar RS. (2022) Wound healing efficacy of novel ayurveda formulation- Pentabark Kashaya: In wistar rats using excision wound model- an in vivo study. *J Ayurveda Integr Med.* 2022 Jul-Sep;13(3):100602.
19. Kumari A, et al. (2022) Wound-Healing Effects of Curcumin and Its Nanoformulations: A Comprehensive Review. *Pharmaceutics.* 2022 Oct 25;14(11):2288.
20. Murugesu S, Selamat J, Perumal V. (2021) Phytochemistry, Pharmacological Properties, and Recent Applications of *Ficus benghalensis* and *Ficus religiosa*. *Plants (Basel).* 2021 Dec 14;10(12):2749.
21. Assar DH, et al., (2021) Wound healing potential of licorice extract in rat model: Antioxidants, histopathological, immunohistochemical and gene expression evidences. *Biomed Pharmacother.* 2021 Nov;143:112151.
22. Monika P, et al., (2021) Challenges in Healing Wound: Role of Complementary and Alternative Medicine. *Front Nutr.* 2021 Jan 20;8:791899.
23. Maheswary T, Nurul AA, Fauzi MB. (2021) The Insights of Microbes' Roles in Wound Healing: A Comprehensive Review. *Pharmaceutics.* 2021 Jun 29;13(7):981.
24. Salmerón-Manzano et al., (2020) Worldwide Research Trends on Medicinal Plants. *Int J Environ Res Public Health.* 2020 May 12;17(10):3376.
25. Soni N, Dhiman RC. (2020) Larvicidal and antibacterial activity of aqueous leaf extract of Peepal (*Ficus religiosa*) synthesized nanoparticles. *Parasite Epidemiol Control.* 2020 Jul 20;11:e00166.