Bioactive Potential of *Ficus religiosa* L.: A promising medicinal plant for Wound Healing and Antimicrobial Resistance

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Abstract

Wound infections pose a significant global health challenge, often leading to delayed healing, increased morbidity, and the emergence of antibiotic-resistant pathogens. The study of plant-based medications involves a wide spectrum of biological activities. Due to the existence of secondary metabolites, medicinal plants has been used and practiced throughout history for the treatment of both acute and chronic conditions. Medicinal plants offer a promising alternative or complement to conventional treatments. Medicinal plants have been acknowledged for many years and are extensively employed worldwide as a significant source of therapeutic compounds for preventing diseases and ailments. Traditional herbal treatments are highly valued among many rural or indigenous people in many nations. Synergistic effects of medicinal plants have garnered significant interest due to their potential to enhance therapeutic efficacy while minimizing side effects.

Keywords: Antimicrobial resistance, Conventional treatment, Plant based medication, Wound healing.

Introduction

Since ancient times, plants have significantly contributed to human health maintenance. Plants being a significant source of human food, have underpinned various traditional and folk medicines for thousands of years. Evidence of humans utilizing medicinal plants for medical purposes traced back to prehistoric period. Until now, 35,000 plant species have been globally used as valuable medicinal agents for disease treatment and prevention. A substantial body of knowledge concerning the promotion of health through the use of medicinal plants has accumulated over the centuries, accessible for today's scientific research on drug discovery [1].The World Health Organization acknowledges the usage of plant extracts or their active constituents in traditional therapies [2].In over 80% of developed nations plants have been utilized as traditional medicine because they provide a rich source of secondary compounds [3]. Medicinal Plants offer a hopeful alternative in the exploration for novel antimicrobials relying on their role in traditional medicine for addressing bacterial diseases and their ability to provide an endless variety of chemical compounds for analysis[4]. Plants hold significant promise for wound management and treatment. Many countries' tribal traditions and folklore have employed a significant number of plants for wound and burn treatment. These natural substances promote healing and tissue regeneration through different mechanisms. These phytomedicines are both affordable and safe. These phytochemicals components found in plants have motivated scientists to investigate their possible properties for wound healing [5].

The traditional systems of medicine are gaining benefits in healthcare due to lower side effects, effective treatment for several chronic diseases, and high expense of new drugs [6]. In traditional medicine, various parts of plants are used to combat infections have been shown to hinder the growth and virulence of different microbes [7].

Skin and Wound Infection

Skin is one of the biggest organs in the body which has three layers epidermis, dermis and hypodermis [8]. Skin is the first line defense mechanism, which acts as a physical barrier. The skin immune response reacts after wounding and infection [9]. Wound infections are the commonest and most troublesome disorder of wound healing [10]. Wound is the breakage of skin which leads to the disruption in the continuity of the epithelium, Along with potential loss of underlying connective tissue. Various factors like physical, chemical, thermal, microbial and immunological agents may be responsible for causing wound infection in humans [11]. Most wound infections are caused by the microbes from the individual's which is present on the skin, mucous membrane, or hollow viscera. Gram-positive cocci, predominantly Staphylococcus aureus, are the typical pathogen found on the skin and mucous surface [12]. Through the years of research and development, significant achievements have been made in the efficiency and precision of wound infection diagnostics [13].

Wound & Wound Healing

According to the World Healing Society, a wound is an injury to the skin, leading to a disruption in its normal structure and function. A wound results from disruptions in the skin's cellular, anatomical, and functional integrity of skin due to chemical, physical, microbial, thermal and immunological factors, leading to damage of the underlying normal tissue [14]. Wounds have been classified into acute and chronic depending on their healing process. In acute wounds, an orderly and time-reparative phase usually leads to sustainable restoration of both anatomical and functional integrity. Acute wounds result from cuts or surgical incisions. Chronic wounds remain in a state of inflammation due to an interruption in the normal healing process. They require a longer time to recover [15,16]. The wound healing process is characterized by a coordinated sequence of processes that includes connective tissue repair and progresses through phases of haemostasis, inflammation, proliferation, and remodeling, during which growth factors, various cells and cytokines collaborate to restore tissue integrity [17]. In wound infection diseases many bacterial and fungal strains are involved and most of these strains become resistant to the most of the synthetic drugs. Skin is colonized with the mixed communities of microbes as normal skin micro biota, mainly constitute of different strains of *Staphylococcus aureus, Corynebacterium,* Yeast etc. from few 100 to several 1000/cm2. Normal skin microbes inhibit pathogens. Trauma, ulcers, burns, surgery or any other damage to the skin broadens its microbial colonization potential. Some of the wound infection pathogens are *Streptococcus sp., Staphylococcus sp., Pseudomonas sp* and *Propionibacterium sp*., from infected wounds. *Candida sp, Malassezia sp*, and *Corynebacterium sp* from non-infected wounds [18].

Antimicrobial Resistance

Antimicrobial resistance (AMR) is a widely recognized worldwide threat, impacting both developed and developing nations. AMR signifies micro-organisms resilience to antimicrobial agents, including anti-fungal and antibiotics. Numerous MDR pathogens have become resistant to all currently existing antibiotics, and they eventually lose their effectiveness against them [19]. Approximately 100,000 tons of antibiotics are produced globally each year, posing a significant risk because of the emergence of resistant gram-negative bacteria [20]. Many of the pathogen strains has developed resistance to antibiotics, they are usually caused by the accumulation of genes on the R plasmid. Each gene is responsible for encoding resistance to a drug. Drug resistance frequently causes delay in receiving effective treatment. The difference between empirical therapy and the resulting antibiotic susceptibility outcomes is the key element in postponing effective treatment [21]. The rising resistance of pathogens to commercially available drugs due to Multi drug resistance has led to an increase in treatment costs, which induces the use of high-cost therapies [22]. Examples of some important MDR bacteria include Carbapenem-resistant Acinetobacter

baumannii (CRAB), XDR (extensively drug-resistant) Pseudomonas aeruginosa, Vancomycin-resistant Enterococci (VRE), Carbapenem-resistant Enterobacteriales (CRE), extended-spectrum, methicillin-resistant Staphylococcus aureus (MRSA) and lactamase (ESBL)-producing Enterobacteriales [23]. Medicinal plants are proved to be effective against multi drug resistant bacteria. Hence they are utilized as medicines to address microbial infection [24]. These Natural antibacterial agents offer benefits in terms of structural and chemical variety, strong effectiveness, accessibility and unique mechanisms of action, while presenting reduced risks of human toxicity and side effects [25]. Over 80% of developing nations rely on plant-based medicines as their primary treatment. Recently, in 2023 the global concern over antibiotic-resistant bacteria's prevalence has grown significantly. The ongoing trend of antibiotic resistance is intensified by the lack of new antibiotic classes emerging, resulting in the "antibacterial crisis" [26].

Role of Medicinal Plants in Wound Healing

Medicinal Plants are more effective in healing wounds as they foster the repair mechanisms naturally; numerous ayurvedic plants have been recognized for their significant role in the wound healing process [27]. Medicinal plants serve as agents for wound healing due to their various components such as flavonoids, tannins, alkaloids, saponins, fatty acids, essential oils, terpenoids, and phenolic compounds, which can enhance the wound healing process. The main advantage of medicinal plants is affordability, availability and minimal side effects. In recent years, researches globally are under process to discover and separate the components from medicinal plants that promote wound healing property [28].

Ficus Religiosa

Ficus religiosa L. commonly referred to as pepal tree is a member of Moraceae family. It is an evergreen tree, smooth when young, found throughout India. They are largely planted along roadside especially near temples [29]. It is often referred to as sacred fig or Ashwattha in Sanskrit. It is among the holy trees revered by Hindus. The various components of the *Ficus religiosa L*. tree, along with its fruits, leaves, bark, seeds, and latex, is utilized in traditional medicine to treat a variety of ailments [30]. In traditional medicinal systems such as Ayurveda, Siddha, Unani, and Homeopathy, this tree plays a significant role due to its traditional uses and pharmacological activities [31].

Traditional Uses

For numerous decades, *Ficus religiosa L*. has been extensively utilized in traditional medicine to address various ailments. Different parts of plants like bark, leaves, fruit and seeds were utilized to cure diseases. It is also used in combination with other herbs. Traditionally, *Ficus religiosa* L. leaves and butter fat were used to treat inflamed ulcer. The dried and powdered fruits were ingested with water for a period of 14 days as part of asthma therapy. It is utilized to address over 50 various conditions such as epilepsy, inflammatory diseases, diabetes, infections, and asthma [32]. *Ficus religiosa* is highly valued in medicinal field due to its numerous compounds that are useful in treatment of various ailments such as respiratory disorders, diabetes, skin diseases, and central nervous system disorder etc [33]. The Unani system of medicine states that the root and bark function as aphrodisiacs and are utilized in the treatment of lumbago. Roots are utilized by individuals suffering from gout and are also chewed to avert gum diseases [34, 35].

Antioxidant Activity

Plants generally contain a wide variety of antioxidant compounds, which play a significant role in the human body. Antioxidants are capable of inhibiting oxidation by terminating radical reactions by donating a minimum of one hydrogen atom to the free radical or by obstructing the start of a radical chain reaction through a substitution reaction [36].The Methanolic extract of *F. religiosa* leaves showed robust antioxidant

capabilities, with an IC50 value of 11.75 µg for scavenging DPPH free radicals, comparable to that of pyrogallol. It demonstrated strong superoxide scavenging ability. The IC50 value at 50.65 µg was comparable to that of ascorbic acid, gallic acid and tannic acid at a concentration of 400 µg. It was found to have rich phytochemical content attributed to high antioxidant property [37]. In a study antioxidant property of plant extract was measured using DPPH method that measured the ability of antioxidants present in the solution to neutralize stable free radicals. The peroxide value of extract with 200 µg /ml to 1000 ranged from 6.34% to 13.35% [38]. In another study the methanolic extract of *Ficus religiosa* leaves showed high flavonoid and phenolic content with indicates high antioxidant capacity with a value of 10.50 µg/ml, and reducing power activity of 0.788 [39].

Antibacterial Activity

Microbes refer to microorganisms, such as bacteria, fungi, viruses and others, which can lead to infections and fatal diseases. An antimicrobial agent denotes either natural or synthetic substances which can eliminate or prevent the growth of microorganisms. The increase in multi-drug resistance organisms has intensified the quest for new antimicrobial agents sourced from natural origins like plants [40]. In a study the antimicrobial property of *Ficus religiosa* leaves using agar well disc diffusion against E.coli, Aqueous and Methanolic extract were compared with standard antibiotic streptomycin, to evaluate the zone of inhibition. The study resulted that the inhibition is concentration dependent [41]. Similarly, in another study they determined the antibacterial property using various solvents such as chloroform, petroleum ether, aqueous, methanol, and hexane. They were tested against E. coli which was isolated from diarrheal patients using disc diffusion method. Methanol extract showed good activity when compared with methanol and aqueous extracts. While petroleum ether and hexane showed no activity [42].

Wound Healing Activity

It has been reported in a study that when 5% and 10% *F. religiosa* leaf extract lotions were applied on Wistar albino rats using incision and excision wound models for studying wound healing activity. For this, 5% povidone-iodine served as the standard. In the group treated with 10% leaf extract ointment, rates of wound contraction and epithelialization were faster, and skin breaking strength was greater, compared to the control group. Tannins have been found to enhance collagen production, contributing to wound healing [38].

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Conclusion

In conclusion, Medicinal plants represent a valuable resource in the fight against wound healing. Wound infectious remain a significant global health challenge due to the increasing prevalence of antibiotic-resistant pathogens. Medicinal plants with diverse bioactive compounds, offer a promising alternative for managing wound. This review highlights the therapeutic effects of plant extracts and their phytochemicals in enhancing antimicrobial efficacy against wound healing. This combined use of medicinal plants and conventional antibiotics has shown improved antimicrobial activity, reducing resistance development, and enhanced wound healing properties.

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Conflict of interest:

The authors declare no conflict of interests

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