Herbal Gel Preparation for the Treatment of Leprosy: A Comprehensive Review of Formulation

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Abstract

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* that primarily affects the skin, peripheral nerves, and mucosal surfaces. Although multidrug therapy (MDT), as recommended by the World Health Organisation, remains the cornerstone of treatment, complications such as delayed wound healing, persistent inflammation, and neuropathic ulcers can occur. Herbal gels have emerged as promising adjunctive formulations due to their biocompatibility, safety profile, and multifunctional pharmacological properties. Medicinal plants such as Centella asiatica, Azadirachta indica (Neem), and Aloe vera possess documented anti-inflammatory, antimicrobial, antioxidant, wound-healing, and immunomodulatory activities that may aid in the management of leprosy-associated skin lesions. Incorporation of these botanical extracts into gel-based systems offers advantages, including improved patient compliance, enhanced local drug delivery, and reduced systemic side effects. This review provides a comprehensive overview of herbal gel formulation strategies, selection of suitable gel bases, extraction techniques, and evaluation parameters. The findings suggest that herbal gel formulations represent a cost-effective and promising supportive approach for improving skin healing and overall therapeutic outcomes in leprosy management.

Keywords

Leprosy, herbal gel, Centella asiatica, Aloe vera, Neem, wound healing, topical formulation, evaluation parameters, and highlights the potential of herbal gels as safe, skin delivery, cost-effective, and patient-friendly.

Introduction

Mycobacterium leprae is the causative agent of leprosy, commonly referred to as Hansen's disease, a chronic infectious disease that mainly affects the skin, peripheral nerves, and mucous membranes. Patients frequently suffer from nerve damage, delayed wound healing, inflammation, and persistent skin lesions. These side effects underscore the importance of topical supportive therapies that can accelerate healing and mitigate lesion severity.For centuries, traditional systems such as Ayurveda, Siddha, and Unani have utilised herbal medicines to treat various skin conditions. Formulating herbal gels as topical delivery systems has attracted more scientific attention in recent years due to their ease of use, patient compliance, non-greasy nature, and capacity to produce localised therapeutic effects.

Centella asiatica, Neem (Azadirachta indica), and Aloe vera are natural ingredients known for their wound-healing, antimicrobial, antioxidant, and anti-inflammatory properties. Including these botanicals in gel formulations provides a promising complementary option alongside traditional leprosy treatments. This review explores the roles of herbal agents, formulation methods, evaluation techniques, and research outcomes related to herbal gels used in leprosy therapy.

Topical gel formulations are increasingly favoured in herbal drug delivery because they offer several advantages over creams and ointments. Gels are non-greasy, easy to spread, penetrate the skin more effectively, and have a soothing effect. Their high water content enhances patient comfort and supports the efficient release of both hydrophilic and some lipophilic phytoconstituents. Adding herbal extracts to gel systems not only enhances their stability but also facilitates localised delivery of bioactive compounds directly to the targeted area, reducing systemic side effects and improving therapeutic outcomes. Several studies have demonstrated that herbal gels containing Centella asiatica promote collagen synthesis and enhance fibroblast proliferation, aiding rapid wound closure. Neem-based gels exhibit strong antibacterial

and anti-inflammatory effects, while Aloe vera gels improve hydration, reduce irritation, and facilitate tissue regeneration. The integration of these herbs into gel matrices presents a promising approach for managing the cutaneous manifestations of leprosy.

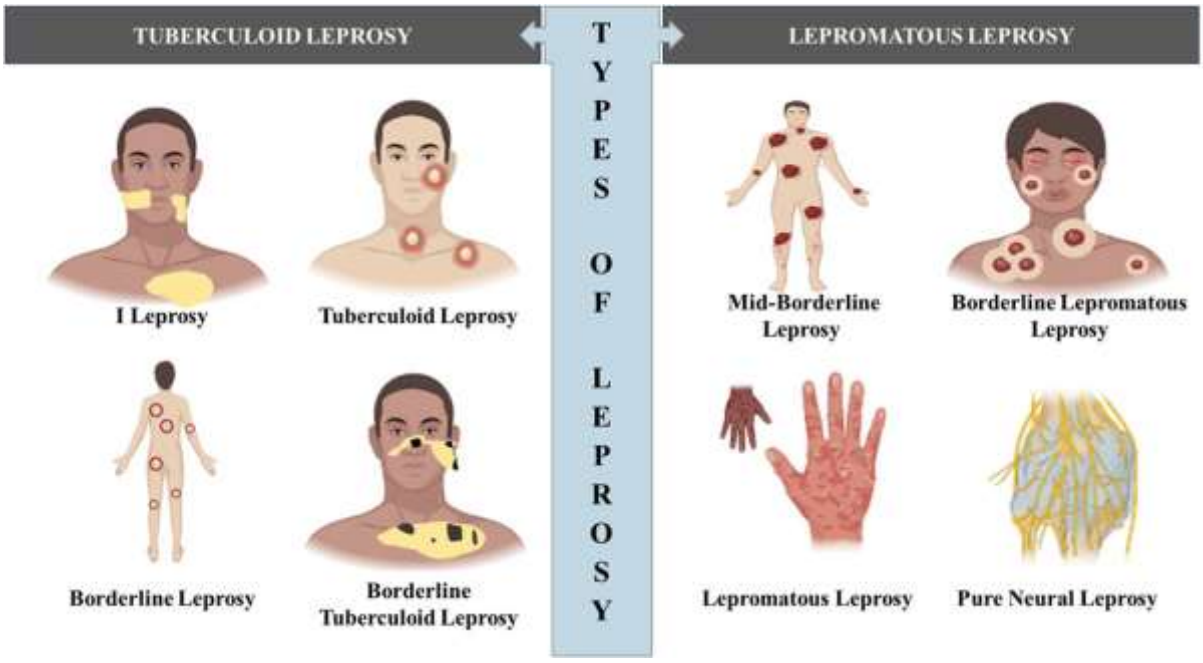
Current Treatment:

MDT, which consists of dapsone, clofazimine, and rifampicin, continues to be the cornerstone of leprosy treatment. Even though MDT successfully reduces the bacterial load, it falls short in addressing secondary issues like skin dryness, delayed wound healing, Type I and Type II inflammation, and the development of chronic lesions. Even after completing MDT, many patients still experience skin degeneration and neuropathic ulcers. Adjunctive treatments that can decrease inflammation and speed up skin repair are, therefore, essential for enhancing quality of life.

Types of leprosy. :

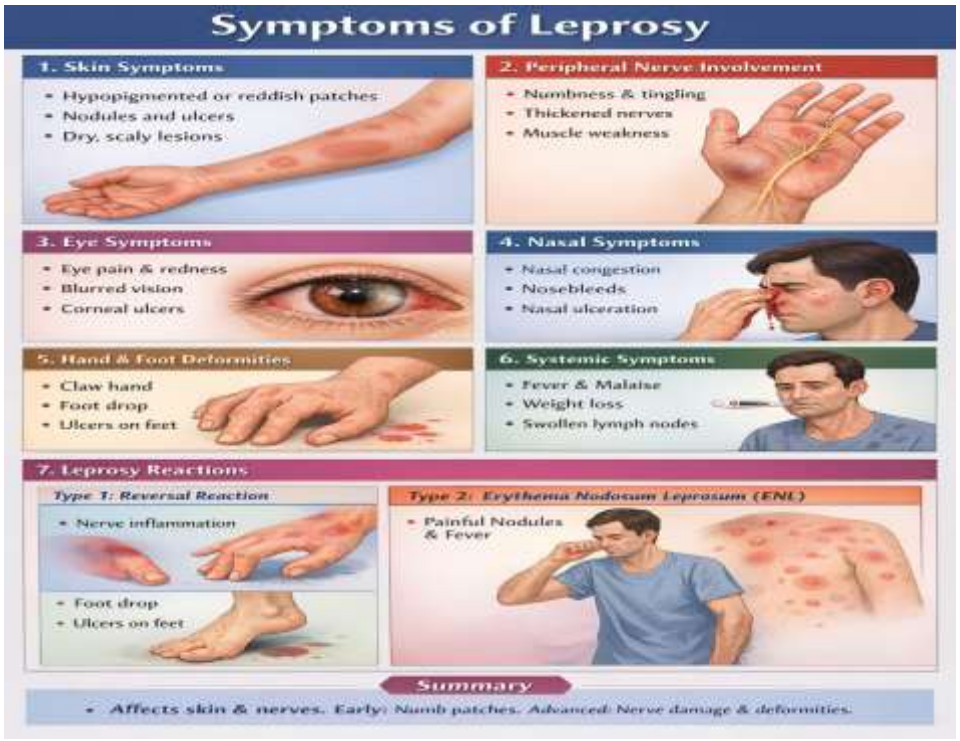
Leprosy is classified into different types based on clinical, histological, and immunological features. The most widely accepted classification is the Ridley-Jopling system,

1. **Tuberculoid leprosy-** Tuberculoid leprosy is a mild form of leprosy caused by *Mycobacterium leprae*. It occurs when the body has a strong immune response against the bacteria, so only a few bacteria are present (paucibacillary type).
2. **Borderline leprosy-** Borderline leprosy is an intermediate form of leprosy caused by *Mycobacterium leprae*, characterised by an unstable immune response and clinical features that lie between tuberculoid and lepromatous types, with variable skin lesions and nerve involvement.
3. **Mid-borderline leprosy** is an intermediate and unstable form of borderline leprosy caused by *Mycobacterium leprae*, characterised by a moderate immune response and clinical features that lie between borderline tuberculoid and borderline lepromatous types.
4. **Borderline lepromatous leprosy**—Borderline lepromatous leprosy (BL) is a form of borderline leprosy caused by *Mycobacterium leprae*, characterised by a weak but not completely absent immune response, with numerous skin lesions and higher bacterial load, showing features closer to lepromatous leprosy**.**
5. **Lepromatous leprosy-** Lepromatous leprosy is a severe and multibacillary form of leprosy caused by *Mycobacterium leprae*, characterised by a very weak or absent cell-mediated immune response, numerous symmetrical skin lesions, widespread nerve involvement, and a high bacterial load.



Symptoms: Leprosy (Hansen's disease) primarily affects the skin, peripheral nerves, mucosa of the upper respiratory tract, and eyes. The symptoms develop slowly due to the long incubation period of the disease. **Skin Symptoms** Skin manifestations are the earliest and most common symptoms of leprosy. Hypopigmented or reddish skin patches with loss of sensation (WHO, 2023) Dry, scaly, and hairless lesions due to damage to skin appendages (Scollard et al., 2006)

Nodules, papules, or plaques, especially in lepromatous leprosy (Walker & Lockwood, 2006) Non-healing ulcers, particularly on hands and feet due to repeated trauma (Talhari et al., 2015) **Peripheral Nerve Involvement: Nerve** damage is a hallmark feature of leprosy. Loss of sensation (pain, temperature, touch) in affected areas (Ridley & Jopling, 1966). Thickened and tender peripheral nerves, commonly ulnar, median, radial, common peroneal, and posterior tibial nerves (Scollard et al., 2006). Muscle weakness and paralysis, leading to deformities such as claw hand and foot drop (WHO, 2023). **Sensory and Motor Symptoms: Numbness** and tingling in hands and feet. Difficulty holding objects. Muscle wasting due to prolonged nerve damage (Walker & Lockwood, 2006). **Eye Symptoms: Ocular** involvement results from cranial nerve damage or direct bacterial invasion. Dry eyes and reduced blinking. Redness, pain, and blurred vision. Corneal ulcers and blindness in untreated cases (Talhari et al., 2015). **Nasal and Respiratory Symptoms:** Nasal congestion and epistaxis (nosebleeds), crusting and ulceration of the nasal mucosa, and septal perforation in advanced lepromatous leprosy (WHO, 2023). **Systemic Symptoms: More** common in lepromatous leprosy. Fever and malaise Weight loss, lymphadenopathy, testicular atrophy and infertility in males (Scollard et al., 2006). **Leprosy Reactions (Acute Episodes**) Type 1 (Reversal reaction): sudden inflammation of existing lesions with nerve pain. Type 2 (Erythema nodosum leprosum): painful nodules, fever, joint pain (Walker & Lockwood, 2006)



Diagnosis:

Leprosy is diagnosed mainly based on clinical features, supported by laboratory investigations. Early diagnosis is essential to prevent nerve damage and disability.

Clinical Diagnosis (Most Important)According to the WHO, leprosy can be clinically diagnosed if one or more of the following cardinal signs are present Hypopigmented or reddish skin lesions with definite loss of sensation Thickened or enlarged peripheral nerves with sensory or motor impairment Clinical examination includes: Testing sensation (touch, pain, temperature)Examination of peripheral nerves (ulnar, median, radial, common peroneal, posterior tibial)Assessment of muscle weakness and deformities

Slit Skin Smear Examination slit skin smear is taken from Earlobes Skin lesions are stained using Ziehl– Neelsen stain, demonstrating acid-fast bacilli (Mycobacterium leprae)

Skin Biopsy (Histopathology)Skin biopsy is used when the diagnosis is doubtful. Findings include: Granuloma formation in tuberculoid leprosy Foamy macrophages (Virchow cells) packed with bacilli in lepromatous leprosy, nerve infiltration and destruction

Lepromin Test (Immunological Test) The Lepromin test assesses cell-mediated immunity. Not a diagnostic test

Molecular Tests (PCR)Polymerase Chain Reaction (PCR) detects M. leprae DNA. Highly sensitive and specific

Nerve Function Assessment, Sensory Testing Muscle power testing, Nerve conduction studies (in advanced cases)

Pathogenesis of Leprosy

Leprosy is a chronic granulomatous infectious disease caused by Mycobacterium leprae, an obligate intracellular, acid-fast prognosis the skin and peripheral nerves. The organism primarily enters the body through the nasal mucosa via respiratory droplets from untreated patients. After gaining entry, M. leprae multiplies slowly due to its long doubling time and preferentially infects macrophages and Schwann cells of peripheral nerves. The incubation period is extended, usually 2 to 10 years, due to the gradual growth of the bacillus. The initial immune response begins with the phagocytosis of M. leprae by antigen-presenting cells (APCs), such as macrophages and dendritic cells. These cells process the bacterial antigens and present them to naïve CD4+ T lymphocytes through major histocompatibility complex class II (MHC-II) molecules in regional lymph nodes. The nature of the host's cell-mediated immune (CMI) response plays a crucial role in determining the clinical spectrum of the disease. A strong Th1-mediated immune response leads to effective control of bacilli, while a weak or absent CMI response results in widespread bacterial proliferation. In tuberculoid leprosy, a robust Th1 immune response predominates. Activated CD4+ Th1 cells secrete cytokines such as interferon-gamma (IFN-γ) and interleukin-2 (IL-2), which activate macrophages to kill intracellular bacilli. This leads to the formation of well-organised granulomas composed of epithelioid cells, Langhans giant cells, and lymphocytes. Although bacterial load is low in this form, the intense immune response causes significant nerve damage due to inflammation and granuloma formation, resulting in sensory loss. In contrast, lepromatous leprosy is characterised by a predominant Th2-mediated immune response. Cytokines such as IL-4, IL-5, and IL-10 suppress cell-mediated immunity and promote humoral immunity, which is ineffective in controlling intracellular pathogens like M. leprae. As a result, bacilli multiply extensively within macrophages, leading to the formation of foamy macrophages (Virchow cells) filled with numerous bacilli. The high bacterial load contributes to diffuse skin lesions and symmetrical nerve involvement. A key feature of leprosy pathogenesis is nerve involvement. M. leprae has a unique affinity for Schwann cells, mediated by specific surface molecules such as phenolic glycolipid-1 (PGL-1), which bind to laminin receptors on Schwann cells. The bacilli invade and replicate within these cells, leading to demyelination and nerve dysfunction. Both direct bacterial invasion and immune-mediated inflammation contribute to nerve damage, resulting in anaesthesia, muscle weakness, and deformities if untreated. Genetic susceptibility also influences disease development. Variations in genes involved in immune regulation, including those related to Toll-like receptors (TLRs), tumour necrosis factor-alpha (TNF-α), and other cytokines, affect the host's immune response to M. leprae. Environmental factors, nutritional status, and close contact with untreated cases further contribute to disease transmission and progression. Thus, the pathogenesis of leprosy is primarily determined by the interaction between M. leprae and the host immune response. The balance between Th1 and Th2 immune mechanisms dictates clinical manifestations, bacterial load, tissue damage, and disease.

Current management

The current treatment of leprosy (Hansen's disease) is based on Multidrug Therapy (MDT), which is recommended by the World Health Organisation (WHO). MDT consists of a combination of three drugs: rifampicin, dapsone, and clofazimine. These drugs are used together to effectively kill Mycobacterium leprae and to prevent the development of drug resistance. Rifampicin is the most powerful bactericidal drug and rapidly reduces the number of bacteria, while dapsone and clofazimine help eliminate remaining organisms and reduce the risk of relapse. MDT is provided free of cost under national leprosy control programs, including in India.

The duration of treatment depends on the classification of the disease. In paucibacillary (PB) leprosy, where the patient has five or fewer skin lesions and a low bacterial load, MDT is given for 6 months. In multibacillary (MB) leprosy, where there are more than five lesions or nerve involvement, treatment is given for 12 months. Recently, India has adopted a uniform three-drug regimen for both PB and MB cases, meaning that all patients now receive rifampicin, dapsone, and clofazimine, which simplifies treatment and improves effectiveness.

In addition to treating diagnosed patients, preventive strategies are also used. Close contacts of leprosy patients may be given a single dose of rifampicin as post-exposure prophylaxis (PEP) to reduce the risk of developing the disease. During the course of treatment, some patients may develop immune reactions known as Type 1 (reversal) reactions or Type 2 reactions (erythema nodosum leprosum). These reactions can cause nerve inflammation and pain and are treated mainly with corticosteroids such as prednisolone. In severe cases, other medicines like thalidomide may be used under strict supervision.

Overall, with proper multidrug therapy, early diagnosis, regular follow-up, and management of reactions, leprosy is a curable disease, and timely treatment helps prevent disability and long-term complications.

Herbal Ingredients Used in the Management of Leprosy

S.no	Ingredients	Scientific name	Family	Chemical constituents	Use	Image
1.	Centella asiatica	Centella asiatica	Apiaceae	Asiaticoside, Madecassoside, Asiatic acid	Skin regeneration, Collagen synthesis	
2.	Neem	Azardirachta indica	Meliaceae	Nimbin Nimbidin, flavonoids, tannins , Salannin.	Anti-inflammatory, wound-healing, immunomodulatory	
3.	Aloe-vera gel	Aloe-barbadensis miller	Asphodelaceae	Aloin, polysaccharide, vitamins, glycoproteins	Soothing agent, moisturising agent	

Conclusion

Herbal gel formulations represent a gentle, natural, and patient-friendly complementary approach that may strengthen conventional therapy and contribute to improved dermatological outcomes in leprosy management. The gel preparations are emerging as a promising supportive treatment option in the management of Leprosy. Medicinal plants such as neem, Aloe vera, and Centella asiatica are rich in natural bioactive compounds that help reduce microbial infection, calm inflammation, and promote faster healing of skin lesions and ulcers.

When these plant extracts are formulated into gel form, they offer several practical advantages. Herbal gels are easy to apply, non-greasy, soothing, and more acceptable for regular patient use. Properly developed formulations demonstrate suitable pH, smooth consistency, good spreadability, homogeneity, and stability, ensuring safety and comfort during topical application. The gel base also allows better contact with the affected area, improving local therapeutic action.

Although multidrug therapy (MDT) remains the essential and primary treatment for leprosy, herbal gel preparations may act as valuable supportive care by enhancing wound healing, reducing irritation, preventing secondary infections, and improving overall patient comfort. Nevertheless, further well-designed preclinical and clinical studies are necessary to confirm their long-term safety, standardisation, and therapeutic effectiveness.

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