RESEARCH PAPER

Plant-Based Antifungal Activity of *Carica Papaya* Against Skin-Infecting Dermatophytes

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How To Cite This Article: Karthiga D, Manisha G, Deepika R, Deepasri G, Deepika K, Dharani R, Anis Kumar M. Plant-Based Antifungal Activity Of Carica Papaya Against Skin-Infecting Dermatophytes. Int J Drug Deliv Technol. 2026;16(27s):536-545. Doi: 10.25258/ijddt.16.27s.64

ABSTRACT
Dermatophytosis refers to fungal infections affecting the skin, hair, and nail, commonly caused by fungal organisms such as Trichophyton, Microsporum, and Epidermophyton. These infections occur more often in tropical regions and are known to produce symptoms like itching, erythema, desquamation, discomfort, among others, which affect an individual's quality of life. While antifungals are commonly used, they come with many limitations, including adverse side effects, expensive prices, prolonged treatment regimen, and emerging drug resistance. To counter these problems, medicinal plants have gained considerable attention due to their bioactive content that produces antimicrobial effects. For instance, the Carica papaya leaves have been shown to contain compounds such as flavonoids, phenolic, enzymes like papain, and other biologically active elements. Therefore, the present study aimed at developing a herbal topical gel from the Carica papaya leaf extracts and assessing its antifungal activity. From the results, it was found that the gel possesses good physical characteristics and inhibits dermatophytes fungi growth during in vitro tests. Furthermore, the mechanism through which antifungal activity was attained involved damaging the fungi cell membrane and disrupting its growth and multiplication process.

Keywords: Carica papaya; Dermatophytosis; Antifungal activity; Phytochemicals; Trichophyton

1. Introduction

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Fungal infections represent a significant global health concern, particularly in tropical and subtropical regions where warm and humid conditions favor fungal growth [1]. Specifically, dermatophytic infections are one of the most common superficial fungal infections affecting the skin, hair, and nails. Dermatophytes are keratinophilic fungi that invade keratinized tissues, leading to infections collectively known as dermatophytosis [2]. These infections are highly contagious and can spread through direct contact with infected individuals, animals, or contaminated surfaces [3]. Dermatophytic infections such as tinea corporis (ringworm) [4], tinea pedis (athlete's foot)[5], and tinea capitis are widely prevalent and can cause discomfort, itching, inflammation, and cosmetic concerns [5]. Although these infections are rarely life-threatening, they significantly impact the quality of life of affected individuals. The increasing incidence of dermatophytosis has been attributed to factors such as poor hygiene, immunosuppression, excessive sweating, and the widespread use of occlusive footwear [6]. Conventional antifungal therapies, including azoles and allylamines, are commonly used for the treatment of dermatophytic infections [7]. However, these treatments are often associated with several limitations such as adverse side effects, high cost, prolonged duration of therapy, and the emergence of antifungal resistance [8]. These challenges have led to a growing interest in the development of alternative therapeutic approaches, particularly those derived from natural sources. Medicinal plants (*Azardica indica*, *Curcuma longa, Eugenia uniflora etc.)* have been widely explored for their antimicrobial properties, owing to the presence of diverse bioactive compounds such as alkaloids, flavonoids, tannins, and phenolic compound [9]. Among these, *Carica papaya*, commonly known as papaya, has gained considerable attention due to its broad spectrum of pharmacological activities, including antimicrobial, anti-inflammatory, and wound healing properties [10]. The leaves of *Carica papaya* are especially rich in phytoconstituents such as papain, chymopapain, flavonoids, and phenolic compounds, which contribute to its therapeutic potential [11]. Recent studies have highlighted the antifungal activity of *Carica papaya* leaf extracts against various dermatophytic species, suggesting its potential as a natural alternative to synthetic antifungal agents.

Therefore, the present review focuses on the antifungal potential of *Carica papaya* leaf extract for the effective management of dermatophytic infections. This review also aims to compile and analyze existing literature on its phytochemical composition, mechanism of action, and therapeutic efficacy against dermatophytes.

2. Dermatophytic Fungi

Dermatophytic fungi, commonly referred to as dermatophytes, are a specialized group of keratinophilic and keratinolytic fungi that infect keratinized tissues such as the skin, hair, and nails [12]. These fungi have the unique ability to utilize keratin as a nutrient source, enabling them to colonize and degrade the outer layers of the host tissue. Dermatophytic infections, collectively known as dermatophytosis, are among the most prevalent superficial fungal infections worldwide, particularly in regions with high humidity and temperature [13].

Dermatophytes are responsible for a wide range of clinical manifestations depending on the site of infection. These include tinea corporis (body), tinea pedis (feet), tinea capitis (scalp), tinea unguium (nails), and tinea cruris (groin) . The infection typically begins with the adherence of fungal spores (arthroconidia) to the keratinized surface, followed by germination and invasion of the stratum corneum. The production of keratinases and other proteolytic enzymes facilitates tissue invasion and colonization . The transmission of dermatophytes can occur through direct contact with infected individuals (anthropophilic), animals (zoophilic), or soil (geophilic). The severity of infection and inflammatory response largely depend on the host immune status and the species of dermatophyte involved. In immunocompromised individuals, these infections may become chronic and difficult to treat.

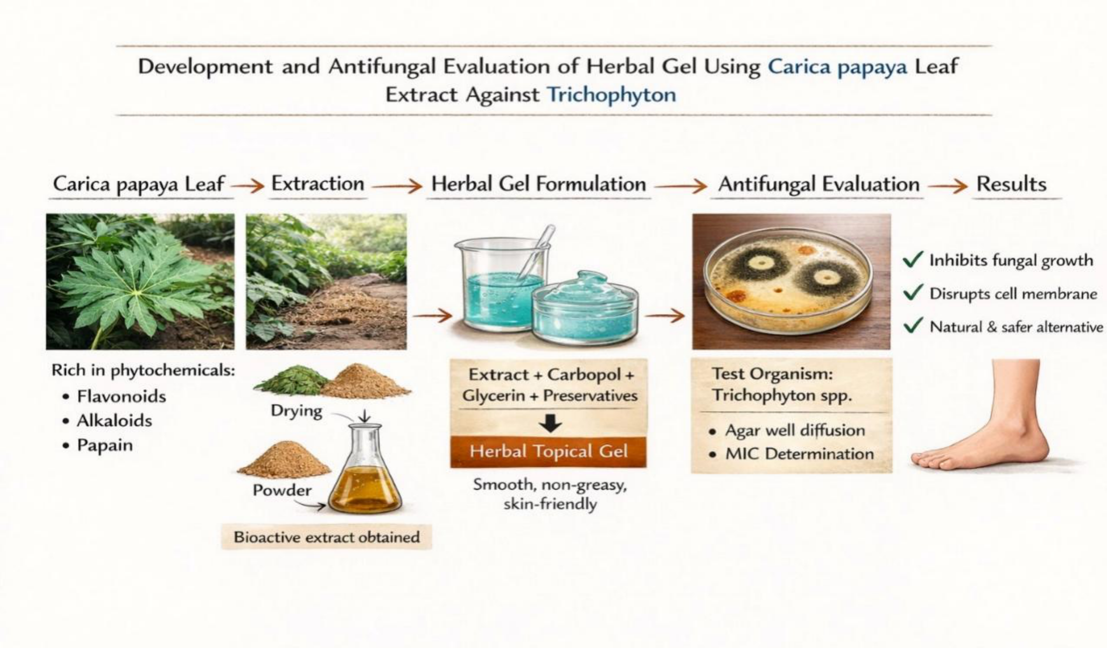

Figure 1: Preparation and antifungal evaluation of carica papaya leaf extract based herbal gel against *Trichophyton spp.*

2.1 Classification of Dermatophytes

Dermatophytes are filamentous fungi belonging to the phylum *Ascomycota* that possess the unique ability to colonize and degrade keratinized tissues such as skin, hair, and nails. The dermatophytes are classified based on morphological characteristics, particularly the structure and arrangement of asexual spores known as macroconidia and microconidia, as well as their ecological niches and host preferences . Based on these criteria, dermatophytes are broadly categorized into three principal genera: *Trichophyton*, *Microsporum*, and *Epidermophyton*. Among these, *Trichophyton* is the most diverse and clinically significant genus, comprising species that infect skin, hair, and nails, and are characterized by the abundant production of microconidia with variable shapes such as spherical, pyriform, or clavate forms [29]. Species such as *Trichophyton rubrum* and *Trichophyton mentagrophytes* are commonly associated with chronic dermatophytic infections in humans and are predominantly anthropophilic in nature, meaning they are well adapted to human hosts and typically cause less inflammatory but persistent infections. In contrast, the genus *Microsporum* primarily infects the skin and hair and is distinguished by the production of large, spindle-shaped macroconidia with rough, thick walls, while microconidia are relatively fewer in number [14]. Species such as *Microsporum canis* and *Microsporum gypseum* are often associated with zoophilic and geophilic habitats, respectively, and tend to induce more inflammatory responses when transmitted to humans due to their non-human origin . The genus *Epidermophyton* is comparatively limited in species diversity and it is unique, produces only macroconidia, which are smooth, thin-walled, and club-shaped, while microconidia are completely absent; the only clinically relevant species, *Epidermophyton floccosum*, infects skin and nails but does not invade hair. In addition to morphological classification, dermatophytes are also categorized based on their ecological distribution into anthropophilic, zoophilic, and geophilic species, which differ in their natural reservoirs, modes of transmission, and degree of host inflammatory response. Furthermore, recent advancements in molecular biology, particularly the use of internal transcribed spacer (ITS) region sequencing and multilocus phylogenetic analysis, have significantly improved the accuracy of dermatophyte classification by revealing genetic diversity and evolutionary relationships among species, leading to the redefinition and identification of several new taxa[30]. Thus, the classification of dermatophytes integrates morphological, ecological, and molecular characteristics, providing a comprehensive framework for understanding their taxonomy, epidemiology, and clinical significance [15].

Figure 2: Ringworm Infection

2.2 Pathogenesis of Dermatophytosis

Dermatophytosis is initiated when infectious fungal elements, mainly arthroconidia, come into contact with keratinized tissues such as the stratum corneum of the skin, hair, or nails, where they adhere to the host surface through specific adhesins and hydrophobic interactions that facilitate colonization. Following successful attachment, the arthroconidia germinate and form hyphae that penetrate the superficial layers of the epidermis, establishing infection [16]. The ability of dermatophytes to invade and persist in these tissues is largely dependent on their capacity to produce a wide array of extracellular enzymes, including keratinases, proteases, lipases, and other hydrolytic enzymes, which collectively degrade structural components of the host tissue and provide essential nutrients for fungal growth. A key factor in this process is keratin degradation, as keratin is a highly resistant fibrous protein stabilized by disulfide bonds, making it difficult for most microorganisms to utilize. Dermatophytes overcome this barrier by secreting sulfite ions that break the disulfide bonds through a mechanism known as sulfitolysis, thereby denaturing the keratin structure and rendering it more susceptible to enzymatic hydrolysis. Subsequently, keratinases and other proteolytic enzymes degrade the keratin into smaller peptides and amino acids, which are then absorbed and metabolized by the fungus [17]. The infection typically remains confined to the outer non-living layers of the epidermis in immunocompetent individuals, as dermatophytes lack the ability to invade deeper tissues; however, the host immune response plays a significant role in determining the clinical outcome, with inflammatory reactions varying depending on the species involved and the immune status of the host. Zoophilic species often induce acute inflammatory responses, while anthropophilic species tend to cause chronic and less inflammatory infections, contributing to their persistence and recurrence. Thus, the pathogenesis of dermatophytosis involves a complex interplay between fungal virulence factors, particularly keratin-degrading enzymes, and host defense mechanisms, which together determine the establishment, progression, and severity of infection.

2.3 Common Clinical Conditions

Dermatophytic infections manifest in various clinical forms depending on the site of infection and the causative species, with the most common conditions including tinea corporis, tinea pedis, and tinea capitis. Tinea corporis, commonly known as ringworm of the body, is characterized by circular, erythematous, and scaly lesions with well-defined borders and central clearing, often accompanied by itching and inflammation; it is primarily caused by species such as *Trichophyton rubrum* and *Microsporum canis* and can spread through direct skin contact or contaminated objects [18]. Tinea pedis, or athlete's foot, is one of the most prevalent dermatophytic infections worldwide, particularly among individuals who wear occlusive footwear or are exposed to moist environments, and is typically characterized by maceration, fissuring, scaling, and itching in the interdigital spaces of the feet; common causative agents include *Trichophyton rubrum* and *Trichophyton interdigitale* [19]. Tinea capitis, which affects the scalp and hair shafts, is more commonly observed in children and presents with symptoms such as hair loss, scaling, inflammation, and in severe cases, the formation of kerion, an inflammatory mass; this condition is mainly caused by species of *Microsporum* and *Trichophyton* and is transmitted through close contact, shared personal items, or infected animals. The clinical presentation of these infections may vary depending on host immunity, environmental conditions, and fungal species involved, but all forms are associated with the ability of dermatophytes to invade keratinized tissues and elicit varying degrees of inflammatory response. Collectively, these common clinical conditions highlight the widespread impact of dermatophytes on human health and emphasize the need for effective antifungal therapies.

3. Medicinal Importance of *Carica papaya*

Carica papaya, commonly known as papaya, is a widely cultivated tropical plant that has been extensively recognized for its diverse medicinal properties and therapeutic applications in traditional and modern medicine. Various parts of the plant, particularly the leaves, fruits, seeds, and latex, are rich in bioactive compounds such as alkaloids, flavonoids, phenolic compounds, saponins, tannins, and proteolytic enzymes like papain and chymopapain, which contribute to its pharmacological activities [20]. The leaves of *Carica papaya* have gained significant attention due to their potent antimicrobial, antifungal, anti-inflammatory, antioxidant, and wound healing properties, making them valuable in the treatment of various infections and skin disorders . The antifungal activity of papaya leaf extract is primarily attributed to the presence of phenolic compounds and flavonoids, which can disrupt fungal cell membranes, inhibit enzyme activity, and interfere with the growth and proliferation of fungal pathogens. In addition to its antimicrobial potential, *Carica papaya* has been traditionally used in the management of fever, digestive disorders, diabetes, and dengue fever due to its immunomodulatory and platelet-enhancing effects. The plant also exhibits significant anti-inflammatory and antioxidant activities, which help in reducing oxidative stress and promoting tissue repair, thereby enhancing its effectiveness in topical formulations for skin infections[21]. Furthermore, the natural origin, low toxicity, and cost-effectiveness of *Carica papaya* make it an attractive alternative to synthetic drugs, particularly in developing herbal formulations such as gels, creams, and ointments for topical application. Recent studies have emphasized its potential role in dermatological applications, especially in combating dermatophytic infections, thereby supporting its inclusion in herbal antifungal formulations. Thus, the wide spectrum of pharmacological activities exhibited by *Carica papaya* highlights its importance as a promising medicinal plant with significant potential in the development of safe and effective therapeutic agents .

3.1 Botanical Description

Carica papaya is a fast-growing, soft-wooded, perennial herbaceous plant belonging to the family Caricaceae, widely recognized for its distinctive morphology and adaptability to tropical climates [22]. The plant typically exhibits a single, erect, hollow, and cylindrical stem that can reach a height of 2 to 10 meters, marked by prominent leaf scars and lacking true woody tissue . The leaves are large, palmately lobed, and deeply divided, measuring up to 60–70 cm in diameter, and are arranged spirally at the apex of the stem, forming a crown-like appearance. *Carica papaya* is generally dioecious, although monoecious and hermaphroditic forms also exist, with male, female, and bisexual flowers borne on separate or the same plants depending on the variety. The flowers are creamy white to yellowish in color, with male flowers typically arranged in long panicles, while female flowers are larger and borne singly or in small clusters close to the stem. The fruit is a large, fleshy berry that varies in shape from spherical to oblong, containing numerous small black seeds embedded in a mucilaginous pulp, and is known for its high nutritional and medicinal value. In terms of distribution, *Carica papaya* is native to Central America and southern Mexico but is now extensively cultivated in tropical and subtropical regions worldwide, including India, Southeast Asia, Africa, and parts of South America, due to its economic importance and favorable growth characteristics [23]. The plant thrives in warm climates with well-drained soils and requires adequate sunlight and moderate rainfall for optimal growth. In India, papaya is widely cultivated in states such as Tamil Nadu, Andhra Pradesh, Maharashtra, and Karnataka, contributing significantly to the agricultural and medicinal sectors. Its widespread distribution and ease of cultivation have facilitated its use in traditional medicine systems across different cultures, thereby enhancing its importance as a valuable medicinal plant.

3.2 Phytochemical Composition

The therapeutic potential of *Carica papaya* is largely attributed to its rich and diverse phytochemical composition, particularly in the leaves, which contain a wide array of bioactive compounds responsible for its pharmacological activities. Among these, alkaloids play a significant role due to their antimicrobial and antifungal properties, with compounds such as carpaine contributing to the inhibition of microbial growth and modulation of physiological functions. Flavonoids are another major class of phytochemicals present in papaya leaves, known for their strong antioxidant, anti-inflammatory, and antimicrobial activities; these compounds can disrupt microbial cell membranes and inhibit enzymatic activity, thereby enhancing antifungal efficacy [24]. Tannins present in *Carica papaya* exhibit astringent properties and contribute to antimicrobial action by precipitating proteins and interfering with fungal cell wall integrity, which ultimately inhibits the growth of dermatophytes. Saponins, which are glycosidic compounds, possess surface-active properties that enable them to interact with cell membranes, leading to increased permeability and eventual cell lysis of microbial pathogens, including fungi. In addition to these secondary metabolites, *Carica papaya* leaves are a rich source of proteolytic enzymes such as papain and chymopapain, which are primarily responsible for the plant's ability to break down proteins; these enzymes not only aid in digestion but also contribute to antimicrobial activity by degrading structural proteins of pathogens and facilitating wound healing [26]. The synergistic interaction of these phytoconstituents enhances the overall antifungal and therapeutic efficacy of papaya leaf extract, making it a promising candidate for incorporation into herbal formulations such as topical gels. Thus, the presence of diverse bioactive compounds in *Carica papaya* underpins its wide range of medicinal applications, particularly in the management of fungal infections .

3.3 Traditional Uses

Carica papaya has been extensively utilized in traditional medicine systems across various cultures due to its wide range of therapeutic properties, particularly in the treatment of skin-related disorders and infections. One of the most notable traditional uses of papaya leaves and latex is in wound healing, where the plant's rich content of proteolytic enzymes such as papain and chymopapain facilitates the removal of necrotic tissue, promotes debridement, and accelerates tissue regeneration, thereby enhancing the healing process. Additionally, the presence of bioactive compounds such as flavonoids, tannins, and phenolic acids contributes to its anti-inflammatory activity by inhibiting the production of inflammatory mediators and reducing swelling, redness, and pain associated with infections and injuries[27]. The antimicrobial properties of *Carica papaya* have also been widely recognized in traditional practices, where extracts of its leaves, seeds, and latex have been used to treat bacterial and fungal infections. These antimicrobial effects are attributed to the synergistic action of phytochemicals that disrupt microbial cell membranes, inhibit enzyme systems, and interfere with microbial metabolism, thereby preventing the growth and spread of pathogens. In many traditional healing systems, papaya leaf extracts are applied topically to treat skin infections, ulcers, and burns, as well as used internally for their immune-boosting properties. The combination of wound healing, anti-inflammatory, and antimicrobial activities makes *Carica papaya* a valuable medicinal plant in ethnomedicine, particularly for managing dermatological conditions and supporting the body's natural defense mechanisms [28].

4. Extraction of *Carica papaya* Leaf

The extraction of bioactive compounds from *Carica papaya* leaves is a crucial step in evaluating their pharmacological potential and formulating effective herbal products, as the efficiency of extraction directly influences the yield and activity of phytoconstituents. The process typically begins with the collection of fresh, healthy leaves, which are thoroughly washed to remove impurities, shade-dried to preserve heat-sensitive compounds, and subsequently ground into a fine powder to increase surface area for solvent interaction. Various extraction methods are employed to isolate phytochemicals, with solvent extraction being the most commonly used technique, utilizing solvents such as water, ethanol, methanol, or acetone depending on the polarity of the desired compounds. Aqueous extraction is widely used in traditional medicine due to its safety and simplicity, whereas organic solvents like ethanol and methanol are preferred in research settings for their ability to extract a broader range of bioactive compounds, including phenolics and flavonoids [17]. Soxhlet extraction is another widely adopted method that allows continuous extraction of compounds through repeated solvent reflux, thereby improving extraction efficiency and yield [18]. The choice of extraction method and solvent significantly affects the composition and biological activity of the final extract, as different solvents dissolve different classes of phytochemicals. Additionally, factors such as temperature, extraction time, solvent-to-sample ratio, and particle size play a vital role in determining the quality and quantity of the extracted compounds. Proper optimization of these parameters is essential to ensure maximum recovery of active constituents while maintaining their stability and biological activity. Therefore, the extraction of *Carica papaya* leaves involves a combination of carefully controlled procedures and conditions to obtain a potent extract suitable for further pharmacological evaluation and formulation into herbal products such as antifungal gels.

4.1 Collection and Preparation

The collection and preparation of *Carica papaya* leaves represent a critical initial step in the extraction process, as the quality of raw plant material significantly influences the yield and efficacy of the final extract. Fresh, mature, and disease-free leaves are typically collected from healthy plants, preferably during the early hours of the day to minimize the loss of volatile compounds and ensure maximum phytochemical content. After collection, the leaves are thoroughly washed with distilled water to remove dust, soil particles, and other contaminants, followed by blotting to remove excess moisture. The cleaned leaves are then subjected to drying, which is usually carried out under shade at ambient temperature to preserve heat-sensitive bioactive compounds such as flavonoids and enzymes, as exposure to direct sunlight or high temperatures may lead to degradation or loss of phytoconstituents. Shade drying also helps in preventing microbial growth while maintaining the integrity of the plant material. Once completely dried, the leaves become brittle and are then ground into a fine powder using mechanical grinders, which increases the surface area for solvent interaction during extraction and enhances the efficiency of phytochemical recovery. The powdered material is typically passed through a sieve to obtain uniform particle size and is stored in airtight containers under cool and dry conditions to prevent moisture absorption and degradation. Proper drying and powdering techniques are essential to maintain the stability, potency, and reproducibility of the plant extract, thereby ensuring consistent results in subsequent extraction and formulation processes.

4.2 Extraction Methods

The extraction of bioactive constituents from *Carica papaya* leaves can be carried out using various methods, among which aqueous extraction, ethanol extraction, and Soxhlet extraction are the most commonly employed techniques, each differing in efficiency and the range of phytochemicals extracted. Aqueous extraction involves soaking or boiling the powdered leaf material in distilled water, allowing water-soluble compounds such as polysaccharides, glycosides, and certain phenolic compounds to diffuse into the solvent, and this method is widely used in traditional medicine due to its safety, simplicity, and cost-effectiveness. Ethanol extraction, on the other hand, utilizes ethanol as a solvent, which is more effective in extracting a broader spectrum of phytochemicals including flavonoids, alkaloids, and tannins due to its intermediate polarity, thereby resulting in extracts with enhanced antimicrobial and antifungal activities; ethanol is also preferred because of its relatively low toxicity and ability to preserve bioactive compounds [27]. Soxhlet extraction is an advanced and efficient technique that involves continuous extraction of compounds using a reflux system, where the solvent repeatedly passes through the plant material, ensuring maximum extraction of both polar and non-polar constituents over an extended period; this method is particularly advantageous for obtaining high yields of concentrated extracts, although it requires longer extraction time and controlled temperature conditions to prevent degradation of heat-sensitive compounds. The choice of extraction method depends on the nature of the target compounds, desired yield, and intended application, as each technique influences the composition, concentration, and biological activity of the final extract. Therefore, selecting an appropriate extraction method is essential to obtain a potent and effective *Carica papaya* leaf extract suitable for antifungal studies and herbal formulation development [17].

4.3 Factors Affecting Extraction

The efficiency and quality of phytochemical extraction from *Carica papaya* leaves are significantly influenced by several key factors, including temperature, solvent type, and extraction time, all of which determine the yield, stability, and biological activity of the extracted compounds. Temperature plays a crucial role in the extraction process, as higher temperatures generally enhance the solubility and diffusion rate of bioactive compounds, thereby increasing extraction efficiency; however, excessive heat can lead to the degradation of thermolabile constituents such as flavonoids and enzymes, ultimately reducing the therapeutic value of the extract. The choice of solvent is another critical factor, as different solvents vary in polarity and thus selectively extract different classes of phytochemicals; polar solvents like water are effective for extracting hydrophilic compounds, whereas organic solvents such as ethanol and methanol are more efficient in extracting a wider range of compounds including phenolics, alkaloids, and flavonoids, which are often responsible for antimicrobial and antifungal activities. Additionally, extraction time influences the extent of compound recovery, as longer extraction periods allow for greater interaction between the solvent and plant material, leading to increased yield; however, prolonged extraction may also result in the co-extraction of unwanted compounds and possible degradation of sensitive phytochemicals due to extended exposure to environmental conditions. Therefore, optimizing these parameters is essential to achieve maximum extraction efficiency while preserving the integrity and bioactivity of the phytoconstituents, which is particularly important for the development of effective herbal formulations such as antifungal gels derived from *Carica papaya* leaf extract.

5. Antifungal Activity of *Carica papaya*

The antifungal activity of *Carica papaya* has been widely investigated due to its rich composition of bioactive phytochemicals that exhibit significant inhibitory effects against a variety of fungal pathogens, including dermatophytes [23,34]. Extracts obtained from papaya leaves, seeds, and latex have demonstrated notable antifungal efficacy, primarily attributed to the presence of compounds such as flavonoids, alkaloids, phenolics, and proteolytic enzymes, which act synergistically to disrupt fungal growth and survival. These phytoconstituents exert their antifungal effects through multiple mechanisms, including alteration of fungal cell membrane permeability, inhibition of essential enzymatic pathways, and interference with nutrient uptake, ultimately leading to cell death. In particular, phenolic compounds and flavonoids are known to damage the integrity of fungal cell walls and membranes, causing leakage of intracellular components, while alkaloids interfere with metabolic processes and enzyme activity within fungal cells [22]. Additionally, proteolytic enzymes such as papain contribute to antifungal action by degrading structural proteins of the fungal cell, thereby weakening the pathogen's ability to invade and colonize host tissues. Several in vitro studies have reported that *Carica papaya* leaf extracts exhibit significant zones of inhibition against common dermatophytic species such as *Trichophyton rubrum* and *Microsporum gypseum*, indicating their potential as effective antifungal agents [34]. Moreover, the natural origin, low toxicity, and broad-spectrum antimicrobial activity of *Carica papaya* make it a promising candidate for the development of alternative therapeutic formulations, particularly topical applications such as herbal gels for the treatment of dermatophytic infections. Thus, the antifungal potential of *Carica papaya* highlights its importance as a valuable medicinal plant in the search for safer and more effective antifungal therapies [24,34].

Table 1: Antifungal Activity of *Carica papaya*

S.No	Parts of Papaya	Fungi	Activity (MIC)	Bio compound Responsible	Effective Concentration	References
1.	Seed oil	*Candida tropicalis*	32–64 µg/mL	Benzyl isothiocyanate	50 µg/mL	29
2.	Fruit	*Microsporum canis*	1000 µg/mL	Xanthosine, Decanoic acid	1 mg/mL	30
3.	Leaf extract	Trichophyton rubrum	125–250 µg/mL	Flavonoids, Phenolics	200 µg/mL	31
4.	Leaf extract	Trichophyton mentagrophytes	100–200 µg/mL	Alkaloids, Tannins	150 µg/mL	32
5.	Latex	Candida albicans	64–128 µg/mL	Papain, Chymopapain	100 µg/mL	33
6.	Seed extract	Aspergillus niger	250–500 µg/mL	Benzyl isothiocyanate	300 µg/mL	34
7.	Peel extract	Microsporum gypseum	500 µg/mL	Phenolics	500 µg/mL	35
8.	Leaf extract	Candida albicans	125 µg/mL	Flavonoids, Saponins	150 µg/mL	36
9.	Seed oil	Trichophyton rubrum	64–128 µg/mL	Fatty acids	100 µg/mL	37
10.	Latex	Aspergillus flavus	200–400 µg/mL	Proteolytic enzymes	250 µg/mL	38
11.	Leaf extract	Microsporum canis	150–300 µg/mL	Phenolics, Tannins	200 µg/mL	39
12.	Seed extract	Candida albicans	100–200 µg/mL	Alkaloids	150 µg/mL	40
13.	Fruit extract	Aspergillus niger	500–1000 µg/mL	Organic acids	750 µg/mL	41
14.	Leaf extract	Trichophyton tonsurans	200 µg/mL	Flavonoids	200 µg/mL	42
15.	Latex	Candida glabrata	128 µg/mL	Papain	120 µg/mL	43
16.	Peel extract	Aspergillus fumigatus	400–600 µg/mL	Phenolic acids	500 µg/mL	44
17.	Seed oil	Microsporum gypseum	80–160 µg/mL	Fatty acids	100 µg/mL	45
18.	Leaf extract	Candida krusei	150 µg/mL	Flavonoids, Alkaloids	150 µg/mL	46
19	Fruit extract	Trichophyton rubrum	500 µg/mL	Phenolics	500 µg/mL	47
20.	Leaf extract	Epidermophyton floccosum	200 µg/mL	Tannins, Saponins	200 µg/mL	48

5.1 Mechanism of Antifungal Action

Carica papaya exerts antifungal activity through several mechanisms based on the presence of different types of bioactive phytochemicals found in the plant [12,34]. For instance, the effects of flavonoids, phenolics, and saponins found in papaya leaves involve disruption of the fungal membrane by interacting with the cellular lipids causing an increase in permeability and leakage, resulting in death of the cells [34,36]. These compounds also affect cell wall components synthesis, such as chitin and glucans, which consequently weaken the structure of the fungus. Enzyme inhibition also plays an important role, as it involves inhibition of the essential metabolic enzymes of fungi through phenolic and alkaloid components. Other parts of the plant can also have antifungal effects, for example, papaya seeds have BITC, which causes damage to the membrane of fungi along with enzyme function inhibition. Papaya latex has proteolytic enzymes like papain, which destroy the proteins of the cell wall. Fatty acids found in seed oil help in damaging cell membranes and interfering with intracellular processes [22,34,36].

5.2 Studies on Antifungal Activity

Numerous in vitro studies have been conducted to evaluate the antifungal efficacy of *Carica papaya* leaf extracts, commonly employing methods such as the zone of inhibition assay and determination of minimum inhibitory concentration (MIC) to quantify their activity against dermatophytic fungi [22]. The agar well diffusion and disc diffusion methods are widely used to assess antifungal activity, where the extract is introduced into wells or discs on agar plates inoculated with fungal strains, and the resulting clear zones around the extract indicate inhibition of fungal growth; larger zones of inhibition correspond to stronger antifungal activity, reflecting the potency of the bioactive compounds present in the extract. Several studies have reported significant zones of inhibition produced by *Carica papaya* leaf extracts against common dermatophytes such as *Trichophyton* *mentagrophytes* and *Microsporum canis*, highlighting their potential as effective antifungal agents [22]. In addition to qualitative assessment, the minimum inhibitory concentration (MIC) provides a quantitative measure of antifungal activity by determining the lowest concentration of the extract required to inhibit visible fungal growth [28]. MIC values are typically determined using broth dilution methods, which allow for precise evaluation of the extract's potency and effectiveness at different concentrations. Lower MIC values indicate higher antifungal efficacy, suggesting that even small amounts of the extract can effectively suppress fungal growth. The combined use of zone of inhibition and MIC studies provides a comprehensive understanding of the antifungal potential of *Carica papaya* leaf extracts, supporting their application in the development of herbal formulations such as topical gels for the treatment of dermatophytic infections [17,18].

5.3 Comparison with Synthetic Drugs

The antifungal efficacy of *Carica papaya* leaf extract has often been compared with conventional synthetic antifungal drugs to evaluate its potential as an alternative therapeutic agent, particularly in terms of effectiveness and safety [22,34]. Synthetic antifungal agents such as azoles and allylamines are widely used in the treatment of dermatophytic infections due to their strong and rapid fungicidal or fungistatic effects; however, their prolonged use has been associated with several limitations, including the development of drug resistance, adverse side effects, and potential toxicity [7,8]. In contrast, *Carica papaya* leaf extracts, although sometimes exhibiting slightly lower potency compared to standard drugs, have demonstrated significant antifungal activity in various in vitro studies, indicating their capability to inhibit dermatophyte growth effectively, especially when used in higher concentrations or optimized formulations [22,34]. Moreover, the presence of multiple bioactive compounds in papaya extract allows for a synergistic mode of action, which may reduce the likelihood of resistance development compared to single-target synthetic drugs. From a safety perspective, herbal extracts are generally considered safer and more biocompatible, as they are derived from natural sources and tend to produce fewer side effects when used appropriately [33,25]. Synthetic antifungal drugs, on the other hand, may cause skin irritation, allergic reactions, hepatotoxicity, and other systemic effects, particularly with long-term use [7,8]. Additionally, the use of plant-based formulations such as herbal gels can enhance patient compliance due to their mild nature and reduced toxicity. Therefore, while synthetic antifungal agents remain highly effective for rapid treatment, *Carica papaya* leaf extract offers a promising, safer alternative with considerable antifungal potential, particularly for topical applications in the management of dermatophytic infections [22,34].

6. Antifungal Assay Methods

6.1 Antifungal Assay Techniques:

Antifungal assay techniques are applied to test the effectiveness of the Carica papaya leaf extract on dermatophytic fungi [22]. The commonly utilized antifungal assay techniques include agar diffusion techniques (disc and agar well diffusion techniques) [28]. Zonation of inhibition shows the antifungal activity of the test substance. The broth dilution technique is applied to measure MIC, which means the lowest concentration inhibiting the growth of the fungus [25,26]. MFC is the lowest concentration killing fungi.

6.2. Agar Well Diffusion Assay:

Agar well diffusion assay is amongst the most commonly employed techniques for measuring the antifungal activity of plant extracts. In this technique, an agar plate containing various fungal strains is used. Wells are punched out on this agar plate, and the extract to be tested is put into the well. This is followed by a process of incubation wherein compounds diffuse from the well, thereby inhibiting fungal growth and generating a clear zone of inhibition [28].

6.3. Disk Diffusion Test:

Disk diffusion test is a conventional method applied for the assessment of anti-fungal activity. According to this test, filter papers impregnated with extracts are placed in an agar plate infected with fungi. The diffusing chemicals will then produce a zone of growth inhibition around each filter paper disk. The larger the zone, the higher is the efficacy against fungi. This method is quite easy, but the diffusion capability of the chemicals plays an important role in the effectiveness of this test [28].

6.4 Broth dilution technique:

The broth dilution technique is a quantitative method of testing for the presence of antifungal activity by measuring the minimum inhibitory concentration (MIC). This technique involves preparing various concentrations of the extract in a liquid culture medium and then adding fungal strains. The lowest concentration of the test substance that prevents growth is measured and reported as MIC [25,26].

7. Conclusion

The current review focuses on the considerable antifungal potential of Carica papaya leaf extract for treating dermatophytic infections [22,34]. The presence of various secondary metabolites such as flavonoids, alkaloids, tannins, saponins, and proteases like papain provides an antifungal effect to the plant [12,4]. In addition, some researchers have found a number of benefits related to the antifungal, anti-inflammatory and wound healing activities of Carica papaya leaf extract [4,34]. Numerous studies have shown that the plant can exhibit considerable inhibitory activity against different dermatophytic species based on the interference with cell wall integrity, increasing of membrane permeability, and blocking enzymatic processes required for fungal survival and reproduction [22,34, and 36]. There are many benefits associated with using plant extracts as antifungal drugs. Firstly, these agents contain biologically active substances. Secondly, their low toxicity and cost make them promising alternatives to commonly used antifungal compounds [34]. Thirdly, there is no risk of building up resistance to plants. However, several challenges associated with the use of Carica papaya should be noted such as inconsistent phytochemical composition, nonstandardized extraction methods, and problems with stability [17,18].

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