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Onychomycosis: Pathological Hallmarks And Its Herbal Therapeutic Interventions

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Abstract
A frequent nail fungal infection, onychomycosis is mostly brought on by dermatophytes, moulds, and yeasts. Nail discoloration, thickness, and detachment from the nail bed are some of the symptoms that this illness presents with onychomycosis has a complex etiology, with Trichophyton rubrum being the most prevalent pathogen. According to estimates, the incidence of this infection is 5.5% worldwide, and rising rates are linked to ageing populations, lifestyle changes, and urbanization.
Different clinical types of the illness are brought on by fungal invasion that is aided by keratin breakdown. Clinical assessment backed by laboratory testing, such as potassium hydroxide wet mounts and sophisticated molecular methods like PCR, is necessary for diagnosis, with an emphasis on the degree of nail involvement and patient-specific characteristics. treatment approaches range from topical antifungals for mild instances to systemic medicines for more severe infections.
Onychomycosis can now be better managed thanks to recent advancements in diagnostic and treatment techniques, which highlight the significance of prompt intervention in preventing consequences and recurrence. The signs, symptoms, etiology, epidemiology, pathophysiology, classification, diagnosis, differential diagnosis, and available treatments—including cutting-edge therapies like Ayurvedic remedies—are all covered in this paper's thorough discussion of onychomycosis.

Keywords: *Onychomycosis, causative agents, clinical features, Trichophyton rubrum, diagnosis, treatment modalities.*

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I. Introduction

The term onychomycosis refers to a fungal infection of the nail, which may be brought on by different types of fungi such as dermatophytes, molds, and yeasts. It often shows up as changes in the nail, like discoloration (the nail may turn yellow, brown, or white), onycholysis is the lifting between the nail and the nail bed, and thickening of the nail plate [1]. The infection can exist in any area of the nail plate (the hard portion of the nail), the nail matrix (where the nail grows), and the nail bed (the skin beneath the nail) [2]. The term "onychomycosis" originates from the Greek terms "onyx," denoting nail, and "mykes," denoting fungus [3]. The most common disorder affecting the nails, onychomycosis, is responsible for around half of all nail infections [4]. A nail infection can affect the sense of touch in the fingers, and toenail infections can make it hard to walk, exercise, or wear shoes properly. If left untreated, the infection can spread to family members and contaminate shared spaces. The infection can also become long-lasting and hard to treat, with 16-25% of people not getting better with current treatment [5]. Recently, new methods have been developed to more precisely and successfully identify onychomycosis, as well as new therapies for the illness. This update aims to inform readers about the latest ways to diagnose and treat onychomycosis [6, 7].

Sign and Symptoms

- The symptoms of a fungal nail infection include thicker nails, crumbling, and a change in color. Sometimes the skin around the nail may also look thickened or scaly.
- A fungal infection can impact several nail sections. Usually, it starts at the sides and tip of the nail. Sometimes, the top layer of the nail may have white marks. In rare cases, the infection starts near the nail base.
- Fungal nail infections can sometimes be painful, and if they affect the toenails, they may make it hard to walk [8].

Global prevalence

According to research that uses patients as the unit of analysis, the global prevalence of onychomycosis is estimated to be 5.5%. According to earlier estimates, onychomycosis accounts for 50% of nail diseases and has a global frequency of 2% to 8%. Instances according to these earlier figures, onychomycosis prevalence was found to be 8.9% in hospital-based studies and 4.3% in population-based studies [9]. Evidence suggests that the frequency is increasing, which could be credited to factors including increased urbanization, occlusive contemporary shoes use, higher life expectancy, and obesity prevalence [10]. Older people are at greater risk to have onychomycosis, and the disorder becomes worse as people age [11]. Found a prevalence of 0.44% in children of North America [12]. Onychomycosis is becoming more common, in part because of rising rates of diabetes mellitus, HIV infection, and increased usage of ageing populations and immunosuppressive drugs. It should come as no surprise that common risk factors like using showers and changing rooms in swimming pools create warm, humid microenvironments that are perfect for the growth of several fungi. Risk factors also include residing with relatives who have onychomycosis, psoriasis, tinea pedis, and immunodeficiency [6].

II. Etiology

Although *Trichophyton rubrum* is the most typical cause of onychomycosis, it can also be brought on by other dermatophytes, such as *Trichophyton mentagrophytes* and *Epidermophyton Floccosum.* Dermatophytes are seen in 50% of instances of onychomycosis in the fingernails and 90% of cases in the toenails [13]. Non-dermatophyte moulds that can result in onychomycosis include *Fusarium species*, *Aspergillus species*, and *Scopulariopsis species*. *Acremonium species* and *Alternaria species* [14]. Worldwide, non-dermatophyte moulds are responsible for about 10% of instances of onychomycosis [15]. About 70% of yeast-induced onychomycosis results from *Candida albicans* [16]. *Candida tropicalis* and *Candida parapsilosis* are examples of other species of Candida [17]. It is more common for patients with immunodeficiency and chronic mucocutaneous candidiasis to get the yeast infection, particularly in their fingernails [18, 9].

III. Anatomy Of Nail

A review of the nail unit's anatomy and the nail may benefit from the growth process to better understand the pathophysiology of dermatophytic fungus within the nail unit. Figure 1 shows the nail unit diagram. Its constituent elements are the nail plate (also called the nail), cuticle, matrix, proximal and lateral folds, nail bed, and hyponychium. The cuticle, the horny layer of the nail fold at the proximal that shields the nail matrix from infection, is made up of a modified stratum corneum. The nail matrix is where the nail grows. The nail plate is formed by the division, differentiation, and keratinization of nail matrix cells as the nail grows. The lunula is the visible, crescent-shaped region near the nail's base. At the base of the nail, the matrix extends 5 mm beneath the skin. The largest portion of the nail, the nail plate, develops by pushing forward over the nail bed. As it grows, the tip of the nail eventually lifts off the bed of nails. Fingernails grow about 2 to 3 mm each month, while toenails grow around 1 mm per month. This means it takes roughly 6 months to develop a new fingernail and 12 to 18 months to develop a new toenail. This growth rate is frequently slowed in older people with onychomycosis and peripheral vascular disease.

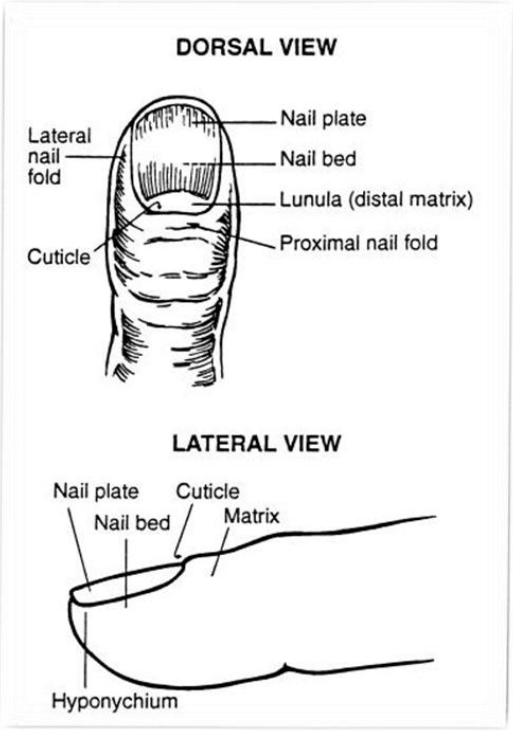

Figure 1: Anatomy of nail [19]

IV. Pathogenesis

Onychomycosis can occur when dermatophytes, non-dermatophyte moulds, or yeasts make contact with the nail directly. The nail unit is vulnerable to fungal infection due to its inadequate cell-mediated defense [10]. In the nail plate, keratin is broken down, and the fungus produces enzymes with lipolytic, keratinolytic, and proteolytic characteristics that aid in fungal nail infection. The location and invasion pattern result in the emergence of various clinical symptoms of onychomycosis. In addition to facilitating penetration into tissues, proteinases break down keratin, giving the fungi nourishment [20]. Fungal biofilm development contributes to antifungal resistance by enabling the fungus to elude existing antifungal treatments [21].

V. Classification Of Onychomycosis

There are five types of onychomycosis, which are classified based on how they appear and how as the illness spreads [22].

Distal Subungual Onychomycosis

Distal subungual onychomycosis, is the most prevalent type of nail fungus both the nail's base and its bottom are affected after it begins beneath the nail tip [Fig-2]. The fungus moves upward through the nail's root area. The causes mild inflammation, leading to abnormal skin cell buildup and thickening under the nail. Consequently, two things happen: the nail may lift away from the bed of nails (onycholysis), and the area under the nail becomes thicker. The area under the nail can become a place where harmful bacteria and moulds grow, causing the nail to turn yellowish-brown.

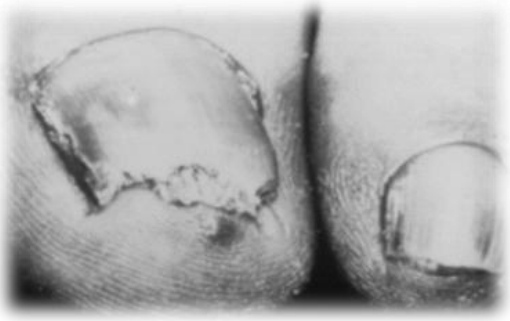

Figure 2: onychomycosis at the distal end [19]

This type of infection is typically brought on by *Trichophyton rubrum*, with *Trichophyton mentagrophytes* being less common [23, 20].

Proximal Subungual Onychomycosis

A less prevalent kind of nail fungus is proximal subungual onychomycosis (PSO), sometimes known as proximal white subungual onychomycosis (PWSO) [19]. PSO can appear as patches or as horizontal stripe-like patterns. Traditionally, the infection is seen starting from beneath the base of the nail and the surrounding skin [fig 3] [22]. When the fungus first infects the area beneath the cuticle and then moves towards the nail tip, it causes proximal subungual onychomycosis [11]. The usual causes of this kind of illness are *Fusarium species* and *Trichophyton rubrum* [23]. Proximal subungual onychomycosis is more common in those with weakened immune systems, especially those with AIDS [11].

Figure 3: Proximal subungual onychomycosis

White Superficial Onychomycosis

The fungus, usually *Trichophyton mentagrophytes*, affects the nail's upper surface in white superficial onychomycosis. White spots or patches on the nail's surface are typically indicative of white superficial onychomycosis [fig. 4] [23]. The white spots and patches can be easily wiped away [24].

Figure 4: White superficial onychomycosis [17]

Endonyx Onychomycosis

A fungal illness called endonyx onychomycosis affects the nail bed, but not the nail plate. This type of infection is very rare and is usually caused by *Trichophyton soudanense* and *Trichophyton violaceum*. Endonyx onychomycosis typically shows as milky patches on the nail plate, grooves, and layers of the nail separating [Fig. 5]. The nail plate stays tightly attached to the nail bed, and under the nail, the skin does not thicken [17].

Figure 5: Endonyx onychomycosis [17]

Total Dystrophic Onychomycosis

Complete nail damage characterizes total dystrophic onychomycosis, which is frequently the last stage of onychomycosis and can appear after any of the other forms [25, 17]. Total dystrophic onychomycosis appears as a badly damaged, crumbled nail that is yellowish, thickened throughout, and brittle [fig. 6] [17, 20]. It can develop from a long-lasting Distal Lateral Subungual Onychomycosis (DLSO) or Proximal Subungual Onychomycosis (PSO).

Figure 6: Total dystrophic onychomycosis [16]

VI. Diagnosis And Diagnostic Studies

Onychomycosis should not be diagnosed based solely on clinical criteria. The diagnosis should be confirmed with lab tests, including growing the fungus from a sample taken from a patient who has not started treatment yet [26]. The most common dermoscopic pattern seen when the nail is splitting is a jagged, spiked proximal edge [11]. Additional dermoscopic observations include a "ruined" look, whitish to yellow lines or streaks, subungual hyperkeratosis, leukonychia (white discoloration), chromonychia (nail discoloration), bands that are parallel to various colors ("aurora borealis"), and dermatophytoma [27].

The diagnosis can be verified by examining the sample under a microscope using a potassium hydroxide (KOH) wet mount, analyzing the afflicted nail tissue with a periodic acid-Schiff (PAS) stain, performing a fungal culture, or using polymerase chain reaction tests. The perfect test would detect the fungus with speed and precision, confirm if it is alive, be simple to perform, provide fast results, be affordable, and have high accuracy and reliability [11, 28].

Dermatophyte DNA in nail samples can be directly detected employing more modern molecular methods as the polymerase chain reaction (PCR). A PCR enzyme immunoassay (EIA) using specific primers for the topoisomerase II gene can identify dermatophytes such as T. rubrum, T. interdigitale, and Epidermophyton Floccosum straight from medical specimens [26].

A potassium hydroxide (KOH) test is a quick and affordable way to check for the presence of fungi, giving results almost immediately [29, 30]. After placing the nail sample on a glass slide, a drop of potassium hydroxide (10-20%) is added. The nail sample is then examined under a light microscope [31]. Keratin is dissolved by potassium hydroxide, making the septate hyphae easier to see. Absent the use of dimethyl sulfoxide, the sample is capable of being slowly heated to accelerate the breakdown of keratin [20]. Yeast cells, spores, and fungal hyphae are seen in a positive test. However, it does not identify the type of fungus or whether it is alive [6, 11, 20]. A potassium hydroxide (KOH) test requires skill to perform and has a sensitivity of 48 to 60% [6, 9, 20].

PCR testing quickly and accurately amplifies fungal DNA bits from fungus [32]. The particular dermatophyte causing the infection can be accurately identified using the PCR method. Furthermore, the results are available in days as opposed to weeks [32, 33]. But PCR tests are expensive and not generally available, which restricts their use in everyday practice [31].

DIFFERENTIAL ONYCHOMYCOSIS DIAGNOSIS

Psoriasis

- Nail lifting (onycholysis), thickened skin underneath the nail (subungual hyperkeratosis), tiny blood spots underneath the nail (splinter haemorrhages), the nail's white discoloration on the nail (leukonychia), and nail deformity (dystrophy)
- Small dents
- An oil drop sign is a translucent yellow-red spot or discoloration seen under the nail
- Other skin symptoms of psoriasis and a family history of the condition

Lichen planus

- Cutaneous disease at other sites
- Thin nails with ridges

- Dorsal pterygium is scarring at the foot of the nail

Trauma
- A nail plate may seem strange
- The nail bed should look normal
- Nail separation at the tip due to repeated injury

Eczema
- Nail that are uneven and curved with ridges
- Skin signs of eczema

Yellow nail syndrome
- The nail looks green-yellow
- Nails are thick and have a raised, curved shape
- The nail may fall off and be painful
- Linked with bronchiectasis, swelling in the legs, and long-term sinus infection

Lamellar onychoschizia
- Typically, the distal part of the nail
- Repeated bathing in water history

Malignant melanoma
- Black discoloration on the nail bed of nails or plate
- Pigment may spread to the fold of the nails
- May experience related bleeding

Myxoid (mucous) cyst
- Cyst at the nail's base and groove running the length of the nail

Alopecia areata
- Brittleness, longitudinal ridging, and pits
- Loss of hair [34]

VII. Treatment

Typical therapy alone is often effective for minimal onychomycosis that doesn't include the matrix. However, a systemic antimycotic medication, usually in combination with a topical one, should be used to treat matrix involvement, which is frequently identifiable by the so-called yellow streaks. The number of afflicted fingernails or toenails, the degree of nail involvement, multimorbidity, medication interactions, and the pathogen found all play a role in determining the best course of treatment (Table 1). Water-soluble ciclopirox olamine nail varnish works better than amorolfine when applied topically [35].

While Fluconazole is the preferred treatment for confirmed candida species Infections, terbinafine, fluconazole, or itraconazole should be used for confirmed dermatophyte infections. Depending on the preparation, therapy can be either continuous or intermittent. Terbinafine produces the highest response rate. Systemic antimycotic medication should only be administered to liver disease patients under specific conditions. Between 20% and 50% of fungal nail infections return within 36 months after therapy concludes [36].

Table 1: In order to treat onychomycosis (Typical duration: 6 weeks for involvement of the fingernails and 12 weeks for involvement of the toenails) [26].

Treatment	Indication	Active agent	Dosing schedule and cure rate
Atraumatic removal of nails	Before receiving a particular treatment	20-40% blockage of urea	Unknown daily cure rate
Antifungal nail polish	Only use monotherapy without matrix involvement if less than half of the surface is impacted and no more than three nails are impacted.	Ciclopirox olamine	48 weeks per day, 58.3%
		Amorolfine	For 48 weeks, once every week, 26.7%
Systemic antifungal therapy	Involvement of more than 3	Terbinafine	For 6-12 weeks, 250 mg qd,

	nails or more than half of the nail area, or if proximal subungual onychomycosis is present		76%
		Itraconazole	200 mg dosage for a week, and then a three-week break, and repeat
			6-12 weeks (IV), 63% 200 mg every day for 6-12 weeks (long-term care), 69%
		Fluconazole	For 3-12 months, 150-300 mg once a week, 48%
Laser therapy	Now under discussion	Different types of lasers	-

Ayurvedic treatment for onychomycosis

Different herbal plants are used for the treatment of onychomycosis which includes:

7.1.1 Guava Leaves
7.1.2 Turmeric
7.1.3 Amla
7.1.4 Beetroot
7.1.5 Heena
7.1.6 Garlic
7.1.7 Clove oil
7.1.8 Pure peppermint
7.1.9 Neem

Guava Leaves

Figure 7: Guava leaves

- **Common name:** Guava leaves
- **Biological name:** *Psidium Guajava*
- **Family:** Myrtaceae

Uses

- Because of their antifungal properties, guava leaves are also commonly utilized.
- Strengthen your immune system.
- Boost the health of your skin [37, 38].

Chemical constituents:

Guava leaves are abundant in bioactive substances, adding to their therapeutic qualities. Important chemical components consist of:

- **Phenolic compounds:** Quercetin, guaijaverin, and other flavonoids are noteworthy for their anti-inflammatory and antioxidant properties [39]
- **Essential oils:** key ingredients with antibacterial and anti-inflammatory properties include 1, 8-cineole, D-limonene, and β-caryophyllene [40]
- **Triterpenoids:** Such as oleanolic acid, which has hepatoprotective and anti-inflammatory qualities [41]

Mechanism of action:

- **Cell membrane disruption:** Guava leaf oil contains β-caryophyllene, which can change the permeability of fungal cell membranes, causing intracellular contents to seep out and cell death of nails.
- **Inhibition of cell wall synthesis:** The fungus's structural integrity may be weakened by guava leaf extracts that disrupt the manufacture of its cell walls.
- **Disruption of Mitochondrial Function:** According to some research, chemicals found in guava leaves may affect fungal mitochondrial function, resulting in energy loss and cell death.

Types of onychomycosis potentially treated by Guava leaf:
- Distal Subungual Onychomycosis
- Proximal Subungual Onychomycosis
- White Superficial Onychomycosis. [42]

Turmeric

Figure 8: Turmeric

- **Common name:** Haldi, Turmeric
- **Biological name:** *Curcuma longa*
- **Family:** Zingiberaceae

Uses
- The coloring agent curcumin longa.
- Reduces inflammation.
- To reduce pain in the abdomen [43].

Chemical constituents:
Numerous bioactive substances can be found in turmeric, such as:
- **Curcuminoids:** The phenolic chemicals that give turmeric its distinctive yellow hue are as follows:

❖**Curcumin:** making up over 77% of all curcuminoids, the major curcuminoid.
❖**Demethoxycurcumin (DMC):** makes up roughly 17%.
❖**Bisdemethoxycurcumin (BMC):** constitutes 3-6%

- **Terpenoids:** Containing the monoterpenes and sesquiterpenes that make up turmeric's essential oils.
- **Phenolic compounds:** Turmeric contains a variety of phenolic chemicals in addition to curcuminoids, which contribute to its antioxidant qualities.

Mechanism of action:
- **Disruption of Fungal Cell Membranes:** It has been demonstrated that components of turmeric essential oil, namely ar-turmerone, prevent dermatophytes from growing by rupturing their cell membranes.
- **Ergosterol is essential to fungal cell membranes:**

❖**Ergosterol works in human cells similarly to cholesterol**

- It maintains the membrane's functionality, stability, and fluidity.
- In the event that the membrane is damaged or ergosterol is reduced:
- The contents of the cell spill out.
- Essential enzymes become inactive
- **Effects:** The fungus dies.

Types of Onychomycosis Potentially Treated
- Distal Subungual Onychomycosis
- White Superficial Onychomycosis. [44].

Amla

Figure 9: Amla

- **Common name:** Indian gooseberry, Amla
- **Biological name:** *Emblica officinalis*
- **Family:** Euphorbiaceae

Ayurveda makes extensive use of EO fruits, which are thought to strengthen immunity to illness. It also works well as an antibacterial and to neutralize snake venom. Cancer, diabetes, liver disease, heart problems, ulcers, anemia, and a host of other illnesses can all benefit from it. Likewise, it is useful as a cytoprotective, antitussive, analgesic, immunomodulatory, antioxidant, and gastroprotective. Tannins, alkaloids, phenolic chemicals, amino acids, and carbohydrates are the main constituents of EO. The maximum amount of vitamin C is found in its fruit juice. There have been reports of EO's antibacterial properties [45].

Chemical constituents:

- **Vitamin C:** Vitamin C content in amla fruits is high; in fruit juice, values of up to 478.56 mg/100 ml have been found.
- **Tannins:** Emicanin A and B, punigluconin, pedunculagin, chebulinic acid, chebulagic acid, corilagin, geraniin, and ellagotannin are among the notable hydrolysable tannins found in it.
- **Flavonoids:** The flavonoids in amla include quercetin and kaempferol.
- **Carbohydrates:** One significant carbohydrate that is found is pectin.
- **Organic Acids:** One of the organic acids found in amla is citric acid.

Mechanisms of action:

- **Antioxidant properties:** Amla is rich in vitamin C and polyphenols, which possess antioxidant effects that can enhance immune function and reduce inflammation, potentially aiding in the management of fungal infections.

Human leukocyte antigen (HLA)-A/B/C expression is significantly downregulated on keratinocytes and melanocytes of the proximal nail matrix (PNM) in comparison to other nail epithelial sections, but HLA-G+ expression is elevated in this area. This may help prevent NK cells from attacking major histocompatibility complex (MHC) class Ia-negative PNM in conjunction with the production of macrophage migration inhibitory factor in PNM.

Types of Onychomycosis Potentially Treatable

- Distal Subungual Onychomycosis
- White Superficial Onychomycosis. [46]

Beetroot

Figure 10: Beetroot

- **Common name:** Chukander, red beet
- **Biological name:** *Beta vulgaris*
- **Family:** Amaranthaceae

Uses

- A coloring agent may be seen in beetroot.
- It could exhibit anti-inflammatory qualities.
- It could aid in weight management [43].

Chemical constituents:

- **Betalains:** These pigments have anti-inflammatory and antioxidant qualities, and they give beetroot its vibrant red and yellow hues.
- **Phenolic compounds:**
- **Vitamins:** Vitamins, including folic acid and ascorbic acid (vitamin C), which are necessary for many body processes, can be found in beetroot.
- **Flavonoids:** Beetroot contains compounds with antioxidant properties, including rutin, epicatechin, and catechin [47].

Mechanism of action:

- **Cell Membrane Disruption**: Extracts from beetroot can weaken the fungal cell membranes, causing cell death and the leaking of internal contents.
- **Enzyme Inhibition**: The chemicals in beetroot may prevent fungal development by blocking enzymes essential for the formation of fungal cell walls.
- **Antioxidant Activity**: By lowering oxidative stress, which is frequently increased during fungal infections, beetroot's antioxidant qualities might boost the body's defences.

Types of Onychomycosis Potentially Treatable

- Distal Subungual Onychomycosis
- White Superficial Onychomycosis [48].

Heena

Figure 11: Heena
(https://images.app.goo.gl/D6xnZbxqGhNQkGhPA)

- **Common name:** Heena tree, lnai
- **Biological name:** Lawsonia inermis
- **Family:** Lythraceae

Lawsonia inermis Linn. It is a member of the Lythraceae family. especially found in arid tropical and subtropical regions, such as India, Sri Lanka, the Mediterranean, and North Africa. This plant, which is generally known as henna India, has been utilised for millennia in traditional medicine and cosmetics. The plant's leaves are mostly used to colour hair, nails, and skin. In several Southeast Asian nations, the plant's powdered leaves are used as an antiseptic for wounds, boils, and some mycotic illnesses in addition to being used as a cosmetic colour. Antioxidant, antidiabetic, hepatoprotective, anticancer, antibacterial, and wound-healing qualities have been discovered in L. inermis's leaves, flowers, seeds, stem barks, and roots. It also has a cooling effect and is used to decrease fevers [45].

Chemical constituents:

- **Flavonoids:** Several flavonoid chemicals, including kaempferol and quercetin, are found in henna. These substances are well-known for their antioxidant qualities, which may support the anti-inflammatory and antibacterial benefits of henna.
- **Tannins:** Polyphenolic chemicals called tannins are found in henna and help give it its astringent qualities. Additionally, tannins contribute to the color shift that happens when henna is applied to the skin or hair.
- **Alkaloids:** Lawsone and methyl lawsone are two alkaloids found in henna that support its antibacterial and maybe analgesic properties.
- **Polysaccharides:** which are complex carbohydrates found in henna, contribute to the plant's capacity to hold onto moisture. For this reason, henna has long been used to treat skin conditions [49].

Mechanisms of action:

- **Lawsone:** Through the disruption of fungal cell membranes and the inhibition of spore germination, this chemical demonstrates potent antifungal actions.

❖**Disrupts fungal cell membrane integrity**

- Lawsone interacts with fungal membrane proteins and lipid bilayers.

❖It causes:

- Destabilisation of membranes
- Intracellular content leakage
- Membrane potential loss
- **Effects:** Fungal cell death

- **Generation of Reactive Oxygen Species (ROS)**
- Lawsone has the ability to infiltrate fungal cells and produce ROS.
- These ROS cause harm:
- Lipids in membranes (lipid peroxidation)
- The proteins
- DNA
- **Effects:** Apoptosis (programmed cell death) with fungal stress

Types of Onychomycosis Potentially Treatable

- Distal Subungual Onychomycosis
- White Superficial Onychomycosis [50].

Garlic

Figure 10: **Garlic**

- **Scientific name:** *Allium sativum*
- **Family:** Amaryllidaceae

Garlic is the popular name for *Allium sativum*, a bulbous plant that is a member of the Amaryllidaceae family. Supposed to have originated in central Asia, it has long been a common seasoning across Asia, Africa, and Europe and a mainstay in the Mediterranean region. Garlic has strong antifungal, antioxidant, and antibacterial properties. The most powerful active anticandidal component was found to be allicin and the volatile oil portion of garlic. Aqueous garlic extract has also demonstrated antimycotic effectiveness against tinea, a common fungal skin infection, capitis, and cruris [51].

Chemical constituents:

- **Flavonoids:** Flavonoids like quercetin, myricetin, and apigenin are found in garlic. These substances are well-known for their antioxidant qualities, which aid in oxidative stress reduction and free radical neutralisation.
- **Phenolic acid:** The compounds found in garlic include p-coumaric acid, ferulic acid, and caffeic acid. These phenolic acids support their antioxidant ability and have been linked to several health advantages.
- **Saponins:** Saponins found in garlic, like eruboside-B, have been associated with a reduction in cholesterol and have antioxidant qualities [52].

Mechanisms of action:

- **Ultrastructural damage:** Garlic oil can enter fungal hyphae cells and their organelles, according to electron microscopy research. This can result in permanent ultrastructural changes, including the destruction of cell organelles and nuclei, which ultimately kills the cell.

❖**Mitochondrial Damage → Energy Collapse**

- Antifungals that harm fungal mitochondria include terbinafine, azoles, and phytochemicals like thymol and lawsone.
- Because ATP generation is blocked, the fungus is unable to maintain vital processes.

- **Effects:** causes cell death and starvation in the fungus.

❖**Vacuole and Membrane Damage → Loss of Osmotic Balance**

- Vacuoles aid in ion storage and detoxification.

❖Here, damage results in:

- Unbalanced ions
- Osmotic oedema
- **Effects:** The fungal cell rupture

- **Antioxidant and anti- inflammatory effects:** By lowering oxidative stress indicators like nitric oxide and malondialdehyde, which are linked to inflammation in fungal infections, garlic extract has shown antioxidant qualities.

Types of Onychomycosis Potentially Treatable with garlic

- Distal and Lateral Subungual Onychomycosis
- Candidal Onychomycosis [53]

Clove oil

Figure 11: clove

- **Synonym:** Clove buds, clove flowers
- **Biological source:** Dried flower buds from *Eugenia caryophyllus* thumb are used to create cloves
- **Family:** Myrtaceae

Essential clove oil contains potent antifungal properties and is herbal medicines and cookery. Its strong aroma makes it suitable for use in aromatherapy, cosmetic, and even dentistry as a natural anaesthetic. Research has demonstrated that it works well against a range of fungal infections, including Aspergillus parasitica and candida albicans; nevertheless, its antifungal properties when administered as a vapour are unknown.

Chemical constituents:

- **Eugenol:** The main ingredient, making around 85–92% of the essential oil of cloves. Eugenol is the compound that gives cloves their distinctive scent and many of their biological properties.
- **Acetyleugenol:** Another component of clove that contributes to its antibacterial and antioxidant qualities is a derivative of eugenol.
- **Eugenyl Acetate:** About 1–15% of the oil is made up of this ester derivative of eugenol, which adds a sweet, balsamic aroma and enhances the fragrance profile overall [54]

Mechanism of action:

- **Inhibition of ergosterol biosynthesis:** The integrity and functionality of the fungal cell membrane are compromised by eugenol's interference with ergosterol production.

❖**Destabilizes the Fungal Cell Membrane**

- Ergosterol gives fungal membranes their structural stability.

❖Blocking its production causes the membrane to:

- Becomes permeable
- Leaky to ions and nutrients
- Cannot maintain homeostasis
- **Effects:** Apoptosis, or programmed cell death, occurs in fungal cells.

❖**Stops Fungal Growth and Replication**

- Fungi cannot develop new membranes without ergosterol, so:
- The production of spores stops
- Colony growth halts
- The infection is contained

- **Effects:** Prevents infection from spreading farther into the surrounding tissue and nail [55].

Pure peppermint

Figure 12: Pure peppermint

- **Synonym:** Pudina, pepper mint
- **Biological name:** *Mentha piperita*
- **Family:** lamiaceae

The antifungal effects of pure peppermint on onychomycosis can be attributed to its main constituents, namely menthol and menthone. Studies have looked at these compounds capacity to stop the growth of several fungus, including those that cause nail infections. Several terpenes and menthol compounds found in pure peppermint may potentially be resonsible for its antifungal properties. Applying these chemicals topically to sick nails helps prevent fungal growth and promote healing. More research is necessary to determine whether pure peppermint is especially helpful in treating onychomycosis, despite the hopeful results [56].

Chemical constituents:

- **Menthol:** This substance, which ranges in concentration from 40% to 50%, is principally responsible for the cooling effect of peppermint oil.
- **Menthone:** Menthone makes up 15% to 20% of peppermint oil's makeup and adds to its minty scent.
- **Menthyl acetate:** This ester, which is found in quantities between 3% and 5%, adds to peppermint oil's distinctive aroma [57].

Mechanism of action:

- **Disrupting cell membranes:** Fungal cell death can result from menthol and menthone interfering with the integrity of fungal cell membranes.
- **Synergistic effects:** The effectiveness of traditional antifungal medications like fluconazole has been demonstrated to be increased when peppermint oil is added.

❖**Membrane Disruption + Increased Permeability**

- When menthol enters the fungal cell membrane, it breaks down lipid bilayers.

❖It causes membranes to leak, which results in:

- Ion and essential molecule loss
- Reduced transport and enzyme activity
- **Effects:** reduces the strength of fungi and improves the penetration of other antifungals (such as azoles and terbinafine).

❖**Biofilm Disruption**

- Dermatophytes such as Trichophyton rubrum are shielded from medications and immune responses by fungal biofilms.
- It has been demonstrated that peppermint oil inhibits and breaks down biofilms, increasing the susceptibility of fungi to antifungal medications.
- **Effects:** improves medication activity and breaks fungal resistance.

Types of Onychomycosis Potentially Treatable with pure peppermint

- Distal Subungual Onychomycosis
- White Superficial Onychomycosis
- Candidal Onychomycosis [58].

Neem

Figure 13: Neem

- **Synonyms:** Margosa, Nimtree, Indian lilac
- **Biological name:** *Azadirachta indica*
- **Family:** Meliaceae

Among the most popular therapeutic plants, neem has a wide range of biological activity and is utilized as a home treatment for many human problems in both homeopathic and ayurvedic medicine. Neem has several active compounds, including nimbidin, nimbin, nimbidol, which have antiviral, antibacterial, antifungal, and anti-inflammatory therapeutic properties [59].

Chemical constituents:

- **Azadirachtin:** One of the best-known bioactive substances in neem, mostly in the seeds, is azadirachtin, a complex tetranortriterpenoid compound with antimicrobial, anti-inflammatory, and anticancer properties as well as insecticidal qualities that make neem oil a natural pesticide.
- **Nimbin:** Neem leaves contain a bitter, antibacterial substance called nimbin. It supports the antipyretic and anti-inflammatory properties of neem. Additionally, nimbin has demonstrated promise in the treatment of inflammatory diseases and infections.
- **Quercetin:** One flavonoid in neem, quercetin, has anti-inflammatory, anti-histamine, and antioxidant qualities. It enhances the immune-boosting and oxidative stress-reducing properties of neem.
- **Glycosides:** Neem's antibacterial, antiviral, and antidiabetic qualities are attributed to glycosides such neemolide and nimbidin [60].

Mechanism of action:

- **Antifungal Action**
  - Fungi are the primary cause of nail infections. Allicin from garlic and nimbidin from neem are examples of sulphur compounds that are fungitoxic, which means they either kill or inhibit fungi. Other sulphur compounds include sulphur (elementary), thiols, and disulphides.
  - They work by:
  - Fungal cell membrane disruption
  - Blocking fungal growth promoting enzymes
  - Preventing fungal cells from synthesizing proteins
  - **Effects:** this slows or stops fungal growth in and under the nail.
- **Antibacterial Properties**
  - Compounds that include sulphur also have broad-spectrum antibacterial action. When bacterial and fungal diseases coexist, sulphur compounds:
  - Disintegrate bacterial biofilms
  - Interfere with the metabolism of bacteria
  - Break through the walls of bacteria and denature proteins
  - **Effects:** By doing this, the injured nail area is shielded from further infections.

Type of onychomycosis potentially treatable with neem

- Distal Subungual Onychomycosis
- White Superficial Onychomycosis [61].

VIII. Conclusion

Onychomycosis is a common fungal nail infection caused by dermatophytes, moulds, and yeasts, leading to symptoms such as nail discoloration, thickness, and detachment from the nail bed. Trichophyton rubrum is the most prevalent pathogen, and the global incidence of onychomycosis is estimated to be 5.5%, with increasing rates linked to factors like ageing populations, lifestyle changes, and urbanization. Diagnosis of onychomycosis requires clinical assessment backed by laboratory testing, such as potassium hydroxide wet mounts and sophisticated molecular methods like PCR, and treatment approaches range from topical antifungals for mild instances to systemic medicines for more severe infections. Recent advancements in diagnostic and treatment techniques have improved the management of onychomycosis, emphasizing the significance of prompt intervention in preventing consequences and recurrence. The classification of onychomycosis includes different types such as distal subungual onychomycosis, proximal subungual onychomycosis, white superficial onychomycosis, endonyx onychomycosis, and total dystrophic onychomycosis, each with distinct characteristics and causative agents. Furthermore, the paper's thorough discussion also covers the available treatments for onychomycosis, including conventional therapies and cutting-edge treatments like Ayurvedic remedies, which have shown promising results due to their antifungal and anti-inflammatory properties. Ayurvedic treatments such as guava leaves, turmeric, Indian gooseberry, beetroot, henna, garlic, clove oil, pure peppermint, neem, and milky latex from *Euphorbia cotinifolia* have been identified for their potential in managing onychomycosis. These natural remedies contain bioactive substances with antimicrobial, antioxidant, and anti-inflammatory effects, making them valuable options for combating onychomycosis.

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