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SHORT REVIEW

Natural Remedies for Onychomycosis: A Review

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Abstract

Onychomycosis, a fungus that causes nail colouring, nail separation, and nail plate growth, has infected the nail unit. There is a chance that the nail structure, nail bed, or nail layer could be infected. The term "onychomycosis" derives from the Greek words "*onyx*" (nail) and "*mykes*" (fungus). Around 50% of all consultations for nail diseases are for onychomycosis, the most common nail infection disorder. About 90% of toenail onychomycosis and 75% of fingernail onychomycosis are caused by dermophytes like *Trichophyton rubrum* and *Trichophyton mentagrophytes*. About 70% of yeast-borne onychomycosis cases are caused by *Candida albicans*. Epidemiological studies that have just been released estimate that onychomycosis affects every community worldwide at a rate of about 5.5 per cent. Onychomycosis is managed in different ways based on clinical categorization, the number of damaged nails, and the severity of the condition. The disadvantages of treatment are that oral therapies are frequently limited by drug interactions and probable hepatotoxicity, and topical antifungals have low efficacy if administered without nail plate biosurgery. The use of plants in medical treatments and herbal therapies is one of the less harmful, cheaper, and widely available alternatives to synthetic pharmaceuticals for treating fungal infections. Undoubtedly, dermatophytes can be inhibited by plant-based extracts as well as essential oils' antifungal activities.

Keywords: Dermatophytes, Essential Oils, Fungus, Herbal, Nail, Plant-based Extract

Abbreviations: American Type Culture Collection (ATCC), Human Immuno Virus (HIV), Minimum Inhibitory Concentration (MIC), Rheumatoid Arthritis (RA)

1. Introduction

Anthropophilic organisms, yeasts, and non-dermatophyte moulds can cause onychomycosis, a fungal disease of the nail unit. The nail plate will become discoloured white or yellow, the nail bed will have hyperkeratosis, the nail plate will dislodge from the nail bed (a condition known as onycholysis), and the nail plate will thicken, crumble, and ridge. With onychomycosis (accounting for 30 per cent of all topical fungal diseases and an approximated 50 per cent of all nail illnesses, it is a significant issue[1]. There are many different onychomycosis prevalence estimates reported in the United States and around the world, but the average occurrence based on population-based research in both North America and Europe is estimated to be 4.3 per cent[2]. With a 20 per cent incidence rate in people over 60 and a 50 per cent incidence rate in people over 70, it is more prevalent in elderly people[3]. Diabetes patients have an onychomycosis rate that is 1.9 to 2.8 times greater than that of the general population[4]. The majority of cases of onychomycosis are caused by anthropophilic organisms, mainly *Trichophyton rubrum* (Jock itch) and *Trichophyton mentagrophytes*[5]. Based on clinical appearance, onychomycosis is split into various subtypes, each of which has a unique set of infecting organisms and forecasts. Onychomycosis has several subtypes, including secondary, shallow endonyx, mixed pattern, complete abnormality, and distal and proximal subungual. The most frequent form of distal and proximal subungual onychomycosis occurs when the pathogenic micro-organism attacks the hyponychium and distal or proximal nail bed. The most frequent organism is *Trichophyton rubrum*, followed by *Trichophyton mentagrophytes*, however, other possibilities include *Candida parapsilosis* and *Candida albicans*. Compared to distal and proximal subungual,

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proximal subungual onycholysis is much less common and is typically brought on by *Trichophyton rubrum*. The fungus penetrates the freshly formed nail plate and enters the proximal nail folds[6]. This occurrence, which is more typical in immunosuppressed patients, should trigger a Human Immuno Virus (HIV) virus test[7]. Total dystrophic onycholysis, which can occur after distal and proximal subungual onychomycosis and is challenging to treat, is the final stage of fungal nail bed invasion[6]. Onychomycosis results in pain, paresthesia, and ambulation issues[8]. Onychomycosis may raise the incidence of foot ulcers in people with peripheral neuropathy and circulatory problems including diabetes, and in extreme cases, can lead to amputation[9]. Patients may also express concerns about their appearance, which could lower their standard of life[10].

A safe and effective treatment method with a low risk of recurrence is preferred due to the impact on the standard of life and medical hazards related to onychomycosis. Unfortunately, there are many reasons for getting proper treatment of nail fungus. First, the distribution of topical and systemic medications to the infection source may be hampered by the thickening of the fingernail and/or the fungal mass. Additionally, the nail plate lacks intrinsic immunity. In addition, leftover cells or colonies that were not previously destroyed may reappear following treatment[11]. Last but not least, lengthy treatment regimens for many topical drugs may restrict patient compliance, particularly in patients who want to apply nail paint for disguise or as cosmetic.

2. Medicinal Plants: As Antifungal Remedy

Herbal antifungal remedies are a less expensive, safer, and more widely available alternative therapeutic treatment for onychomycosis. Plant-based extracts from native species have been shown to have antifungal activity, including actions against dermatophytes, non-dermatophyte moulds, and yeast[12]. Herbal remedies have gained popularity in recent years due to their disease-curing powers and lack of negative effects. Researchers discovered that using plant-based products to combat fungal infections is also a successful strategy. Certain plants, such as ginger root, neem, chives, garlic cloves, tulsi, henna, aloe vera, and others, have been shown to have antifungal efficacy against fungal diseases. Some of the bioactive chemicals discovered in these plants include polyphenols, alkaloids, tannic acid, dihydrogeraniol, geranyl alcohol, thymoquinone[13, 14]. Tanzanian researchers discovered antifungal activity in methanolic foliage and trunk bark extracts of *Euphorbia cotinifolia*. This attractive shrub is used to cure onychomycosis in Tanzania's Kilimanjaro region. *T. rubrum*, *T. mentagrophytes*, and *A. niger* were suppressed by methanolic extracts of *E. cotinifolia* foilage and trunk, while the conventional medicine fluconazole had no effect to prevent the development of these tested fungi. Methanolic extracts of *Euphorbia antiquorum* latex have also been shown to have antifungal action against *Candida albicans, Aspergillus flavus, and Aspergillus fumigatus*[15]. Researchers found that the stem juice of *Euphorbia sanguinea* is utilized locally as a traditional medicine for onychomycosis. When compared to antifungal medications, the sap had strong antifungal action. *E. sanguinea* is the cause for onychomycosis and exhibits antimycotic action against Candida albicans[16]. The antifungal property of sixty- one conventional plant medicines was tested against the onychomycosis-causing dermatophytes fungi *Trichophyton rubrum*. Amongst them many species have shown good anti-fungal activity against *T. rubrum*. Scientists discovered that water and organic extracts of the leaves of *Mitracarpus scaber* and *Pergularia tomentosa* have antifungal activity against the main dermatophytes *T. mentagrophytes, T. rubrum, and M. gypseum* that cause onychomycosis[17].

There are some medicinal plants which are used in treatment of onychomycosis which are discussed in following sections.

2.1 *Allium sativum* (Garlic)

Allium sativum, commonly known as garlic, is a plant species in the Allium genus. It is native to Central Asia and has been cultivated worldwide for its culinary and medicinal properties. The medicinal part of garlic is the bulb, which consists of individual cloves. These cloves are used for various purposes, including as a natural remedy for fungal infections. The primary antifungal compound in garlic is allicin, which is formed when garlic is crushed or chopped. Allicin is not present in intact garlic cloves; it is produced as a defense mechanism against physical damage. Allicin is believed to exert its antifungal activity by disrupting the integrity of fungal cell membranes.

It interacts with thiol (sulfhydryl) groups in various fungal enzymes and proteins, leading to increased membrane permeability and leakage of essential cellular components. This damage compromises the fungal cell's structural and functional integrity, ultimately resulting in fungal cell death. The antifungal activity of garlic or its extracts can be tested using various in vitro laboratory assays. Garlic cloves are crushed, minced, or otherwise processed to release allicin and other bioactive compounds. Extracts can be prepared using solvents like ethanol or water. In the laboratory, fungal cultures are exposed to different concentrations of garlic extract. The growth of the fungus is monitored over a specified period[18]. The antifungal activity is assessed by various parameters, including the inhibition of fungal growth, changes in fungal morphology, and determining the Minimum Inhibitory Concentration (MIC). The MIC is the lowest concentration of garlic extract required to inhibit fungal growth effectively.

Garlic, particularly its active compound allicin, has demonstrated antifungal activity against various fungal species. This includes dermatophytes like *Trichophyton rubrum,* which can cause onychomycosis[19].

2.2 *Origanum Vulgare* Subsp. *Hirtum* (Greek Oregano)

Origanum vulgare subsp. *hirtum*, commonly known as Greek oregano, is a subspecies of wild oregano native to the Mediterranean region. It is well-known for its culinary and medicinal uses. Greek oregano is typically obtained from the leaves and flowering tops of the oregano plant. The leaves are dried and crushed to produce the oregano herb, which is widely used in cooking. Greek oregano, like many other herbs and spices, contains bioactive compounds that may contribute to its anti-fungal properties. One of the key compounds found in oregano is carvacrol and thymol, which has been studied for its antimicrobial and anti-fungal effects. Carvacrol is believed to disrupt the cell membranes of microorganisms, including fungi, leading to cell damage and death. Its showed good antifungal performance against species such as *Trichophyton* spp. and *Malassezia furfur*[20].

2.3 *Cassia alata* Linn.

Cassia alata, commonly known as the candle bush, is a flowering plant native to the American tropics. It is also found in various tropical regions around the world. Extracts from different parts of the candle bush, such as the leaves and stems, are used for various medicinal purposes. *Cassia alata* contains various phytochemicals, including anthraquinones (such as chrysophanol and emodin), flavonoids, and tannins. These compounds are responsible for its medicinal properties. The exact mechanism of action of antifungal properties may involve the presence of anthraquinones and other bioactive compounds. Anthraquinones, in particular, have been studied for their antimicrobial properties, including antifungal effects. They can interfere with fungal cell membranes and disrupt fungal growth processes. *C. alata* extract has been demonstrated anti-fungal activity against *T. mentagrophytes, Fusarium* sp., *Chrysosporium* sp., *Scopulariopsis* sp., *A. terrus*[21].

2.4 *Ageratina pichinchensis*

Ageratina pichinchensis, also known as Pichincha snakeroot, is a flowering plant native to South America, particularly the Andean region. Extracts from various parts of the plant, including leaves and stems, are used for medicinal purposes. *Ageratina pichinchensis* contains a variety of phytochemicals, including alkaloids and flavonoids. A hexane extract from its aerial component has been shown to be effective against *C. albicans, A. niger, T. mentagrophytes* and *Trichophyton rubrum in vitro* cultures of these fungi. It has also been noted, that commonly detected dermophytes in *Tinea unguium* and *Tinea pedis* are resistant to the active ingredient enkephalin. *A. pichinchensis* extracts were therapeutically beneficial on the nails of individuals with moderate and severe onychomycosis[22].

2.5 *Euphorbia cotinifolia* L.

Euphorbia cotinifolia L., commonly known as the Mexican shrubby spurge or tropical smokebush, is a species of flowering plant in the Euphorbiaceae family. It is native to tropical and subtropical regions in the Americas, particularly in Mexico and Central America. It is also grown as an ornamental plant in various parts of the world. The plant is typically grown as an ornamental shrub. Specific phytochemicals present may vary, but Euphorbia species are known for containing a wide range of secondary metabolites, including diterpenes, phorbol esters, and various other compounds. When methanolic extracts of leaves and bark of *E. cotinifolia*

was taken and evaluated it showed antifungal efficacy against *T. rubrum, T. mentagrophytes* and *A. niger*[23].

3. Phytoconstituents and Their Potential Against Onychomycosis

The plant contains a variety of non-nutrient chemical phytoconstituents that are therapeutically bioactive in nature. Phytochemicals like flavonoids, glycosides, polyphenols, saponins, terpenes, alkaloids, aromatic oils, and steroids[24] draw the interest of researchers and the pharmaceutical industry. The extraction of antifungal compounds with antifungal characteristics has now become the natural pattern for the creation of novel medications to treat fungal infections[25]. Rural people from all over the world employed medicinal herbs to treat onychomycosis, which was not well recorded or published because there was no scientific proof of antifungal action. Few studies have been published on the antifungal susceptibility assessments of herbal remedies against dermatophytes that cause onychomycosis, but there is very little scientific information on the antifungal capacity of plants over non-dermatophyte molds[26]. According to study, *Piper regnellii* has a high antifungal capability for treating onychomycosis caused by *T. rubrum*. Although extracted like eupomatenoid-3 and eupomatenoid-5 demonstrated little action against *Trichophyton rubrum* in comparison to the dichloromethane extract. Methanol, hexane, and chilled-water extraction of *Cassia alata, Mitracarpus villosus,* and *Lawsonia inermis* were tested under laboratory conditions for antifungal efficacy against non-dermatophyte molds onychomycosis in rice cultivators in Nigeria. Alcoholic extracts of *L. inermis* shown considerable antifungal properties against *Aspergillus terrus, Aspergillus sclerotiorum, Fusarium* sp., *Chrysosporium* sp., and *Scopulariopsis* sp. at minimum inhibitory concentration ranges of 10-40 mg per disc, and *A. flavus* at a dosage of 40 mg/disc. The findings of this study showed that the existence of Lawsome, natural orange-6 dye like chemicals in the leaves of *Lawsonia inermis* conferred antimycotic ability against fungal infections[26-28].

It was stated that the existence of antifungal capacity of *Schinus terebinthifolius, Piptadenia colubrina, Parapiptadenia rigida, Mimosa ophthalmocentra*, and *Persea americana* plant spp. from Northeast Brazil against *T. rubrum* and *T. mentagrophytes*[12]. It has been discovered that *Piper betle* L. leaf extract has a high antifungal activity against dermatophytes linked with nail infection. The antifungal action of *Piper betle* leaf extract on *T. mentagrophytes* and *Trichophyton rubrum* was checked in comparison with antifungal drugs. Betel leaf extract contains a wide range of phenolic chemicals that have antifungal properties against dermatophytes[29].

Croton tiglium ethanolic extracts were found to have antifungal properties against three dermatophytes, *T. rubrum, T. mentagrophytes,* and *Epidermophyton floccosum*. The results of this investigation revealed that *C. tiglium* stem extract had the maximum inhibitory effect over *Trichophyton mentagrophytes* and *E. floccosum*, but had a lesser activity against *T. rubrum*. The stem extract contained essential compounds like oleic acid and palmitic acid, which were primarily responsible for dermatophyte suppression[30]. Herbal plant extracts demonstrated significant antifungal activity against fungus and can be used as an antimycotic reference for herbal treatment. Furthermore, phytochemicals have also shown to inhibit pathogenic fungus. Naphthoquinones and flavones have been found to be effective antifungal agents in the treatment of nail infections[31].

The flavonoids, coumarins, quinones, lignans, tannins, and neolignans obtained from natural sources exhibit the most promising antifungal potential. Among the known polyphenols, catechins, 3-hydroxyflavones, and tannins have drawn the greatest interest because of their broad range of effectiveness and strong antibacterial properties. According to their basic structural make-up, flavonoids are tricyclic phenylic acid compounds with two arene rings (C6-C3-C6) and a basic skeleton of 15 carbon atoms. A class of natural substances known as flavonoids has antifungal activity in addition to other defensive properties. The subclasses of flavonoids include anthocyanidins, Benzalacetophenone, 3-Benzylchroman-4-One, flavonols, and catechins[32,33]. Flavonols like quercetin, myricetin, and kaempferol have been shown to have action in *C. albicans*. For instance, quercitin, myricetin, and robigenin present in propolis have been shown to have anti-candida action[34]. Gallotannin and the flavanol subclass, both obtained from *Syzygium cordatum*, additionally showed growth-inhibitory characteristics[35]. Baicalein, a subclass of flavones discovered from *Scutellaria*

baicalensis, caused *C. albicans* to undergo necrosis, while apigenin, a flavone obtained from propolis, had antifungal activity. As with coumarins and lignans, flavonoids have demonstrated fungicidal potential against a number of dermatophyte species[32,36].

Tannins are one of the other significant categories of polyphenolic chemicals found in many plant sections, including the roots, foliage, blossoms, fruits, and kernels. They are separated into gallotannins, proanthocyanidins, and hydrolyzable (ellagitannins) condensed tannins[37]. They have both antibacterial qualities and the capacity to precipitate large molecules like proteins[38]. Ellagitannins are a diverse class of polyphenols with a few hexahydroxydiphenate groups that can attach to the glucose molecule in a number of different ways[39]. Elagic, gallagic, punicalin, and punicalagins were isolated from *Punica granatum*, and they showed antifungal activity against *C. albicans, Cryptococcus neoformans,* and *A. fumigatus*[40]. The Brazilian plant *Ocotea odorifera*, which is frequently used in traditional medicine, contains ellagitannins that may be effective towards *C. parapsilosis*[41]. Lambertianin C and sanguiin H-6, two ellagitannins discovered in raspberries, shown fungistatic action both *in vitro* and *in vivo* against *Geotrichum candidum*[42]. Encapsulated tannins from *Acacia mearnsii* have been shown to have moderate efficacy against *A. niger* **and** *C. albicans*[38].

The C3 unit of the C6-C3 skeleton of coumarins contains an oxygen heterocycle[32]. These substances are widely known for contributing to UV tolerance as well as disease and pest resistance. *Aspergillus fumigatus*, *Candida albicans*, and *Fusarium solani* reference strains were used to investigate the antifungal activity of forty coumarins, however only osthenol demonstrated the strongest antifungal activity.

A different coumarin by-product, 4-Methylcoumarin, was successful in suppressing Aspergillus species via altering the virulence factors and the fungal wall structure. Diversinin, a coumarin that was discovered in a *Baccharis darwinii* petroleum ether extract, was fungicidal and showed antifungal efficacy against *T. rubrum, T. mentagrophytes,* and *M. gypsum*. 8-Acetoxy-5-hydroxyumbelliprenin, a different coumarin derivative, was discovered in *Ferula foetida* and demonstrated activity against *M. gypseum* and *Trichophyton interdigitale*[32].

Other naturally occurring substances known as phenylpropanoids, coumarins, and lignans are frequently investigated for their anti-candida effects. Scopoletin, a coumarin, 2-hydroxybenzaldehyde and anisyl alcohol, with minimal inhibitory concentrations of 25, 31, and 31 g/mL, respectively, were discovered to have antifungal properties against *C. albicans*[43,44]. Pyrogallol and curcumin were found to be effective against diverse *C. albicans*[45]. Curcumin also showed anti-biofilm action and reduced the capacity of cells to adhere. Turmeric (*Curcuma longa* L.), which contains curcumin, is a flavonoid. *In vitro* and *in vivo* tests of pure curcumin revealed potential efficacy against *Cryptococcus gattii*[46].

It has been demonstrated that the polyphenol natural component gallic acid, which is found in many species of medicinal plants, has anti-inflammatory and antibacterial activities. A wide range of antifungal activity of gallic acid was discovered against dermatophyte and candida strains. It was established that gallic acid decreases the activities of squalene epoxidase and sterol 14-demethylase P450 (CYP51) in the *T. rubrum* cell membrane. It was showed that *Buchenavia tomentosa's* acetone fraction and the chemical gallic acid it contains have the power to break 48-hour biofilms and impede the adhesion of the reference strains *C. albicans SC 5314* and *C. albicans ATCC 18804*[41].

4. Essential Oils and Their Potential Against Onychomycosis

Many essential oils have been reported for showing therapeutic action against fungus responsible for onychomycosis. These oils might target different pathways as their mechanism of action for the effect. In following section different essentials oils are discussed which has promising effect against onychomycosis**.**

4.1 Clove Oil

Eugenia cariophylata, frequently referred to as clove or *Syzygium aromaticum*, is a Mirtaceae family tree native to the Maluku Islands in eastern Indonesia. Clove trees are often cultivated along the seaside at heights not more than 200 meters above sea level. The growth of blossom buds, that is the commercialized section of the tree, begins approximately four years following the sapling is planted. Flower buds are harvested before flowering during the development stage. The collection can be done chemically or manually with the help of

an organic phytohormone that creates ethylene in the vegetative tissue and promotes early maturation. Indonesia, India, Malaysia, Sri Lanka, Madagascar, and Tanzania, particularly the island of Zanzibar, are the leading producers of cloves today[47]. Several studies have found that fragrant herbs like cinnamon, oregano, clove, thyme, and mint have antimicrobial, antiviral, anticancer, and antifungal properties. However, due to its significant antibacterial and antioxidant properties, clove has attracted a lot of interest among other spices[48].

Clove is mainly composed of phenolic compounds that include hydroxybenzoic acids, flavonoids, hydroxyphenyl propane, hydroxycinnamic acids, and eugenic acid, the main bioactive molecule, as well as gallic acid derivatives such as hydrolysable tannins, which are present in significant amounts in the fresh plant, according to pharmacological research. Additionally, clove contains phenolic acids such as ferulic, caffeic, ellagic, and salicylic acids, as well as flavonoids such as quercetin and robigenin. eugenic acid, acetyl eugenol, and β-caryophyllene account for up to 18 per cent of the essential oil detected in clove flower buds[49].

Clove oil is generally pale yellow in colour. The antifungal activity of clove essential oil and its main component, eugenic acid, against *Candida, Aspergillus*, and *Dermatophyte* and American Type Culture Collection (ATCC) strains was evaluated using minimal inhibitory concentrations and minimum fungicidal concentrations determined according to Clinical and Laboratory Standards Institute regulations. All of the studied strains were inhibited by the clove oil and eugenol. Flow cytometric and suppression of ergosterol synthesis experiments were carried out to understand its mode of effect on yeasts and filament like molds. The concentration of ergosterol, a specific component of the fungal cell membrane, was likewise dramatically decreased by clove oil and eugenol. Below the minimal inhibitory concentration values, oil and eugenic acid levels completely or almost entirely stopped the growth of *Candida albicans* germ tubes[50]. The antifungal and anti-yeast action of eugenol against mold and yeast species isolated from onychomycosis is significant.

4.2 Tea Tree Oil

Melaleuca alternifolia is a small tree or shrub with a bushy crown that can grow tall. Its bark is papery. This tree is native to Australia, where it naturally grows in the northern New South Wales coastline region. Because the species is unique to Australia, the oil is known as Australian tea tree oil. The biological activities of tea tree oil have been demonstrated to include antibacterial, antifungal, antiviral, anti-inflammatory, anti-cancer, a pain reliever pesticidal, and herbicide effect. Steam distillation is used to remove tea tree oil from the foliage and terminal branches. The component is used in a variety of compositions, such as virgin oil, ointments, wart paint, zit medications, and household products including fabric softeners, laundry detergent, and cleansers. Additionally, the oil is used to treat several cutaneous, respiratory, genitourinary, and fever-related illnesses as well as to treat chicken pox, flu, and other infectious infections[51].

Monoterpenoids, sesquiterpenes, and the corresponding alcohols make up the majority of the oils' over 100 different constituents. The main active ingredient in oil is 4-Carvomenthenol, which has an alcoholic group in its structure. The irritating Eucalyptol follows 4-Carvomenthenol. Six oils with different chemical compositions, constitute tea tree oil. There are four sub species of Eucalyptol, as well as sub species for terpinolene and 4-Carvomenthenol. Tea tree oil quality is significantly impacted by the quantity of constituents in oil. Most typically, oil low in Eucalyptol and high in 4-Carvomenthenol is preferred. Tea tree oil with a significant cineole level has a fragrance that is very similar to gum tree oil[52].

4-Carvomenthenol is the primary active component of the oil intricate chemical mixture. Attention has been given to its antiviral, anti-inflammatory, and antifungal properties[52]. *Candida albicans* may assume on a variety of morphological forms, such as yeast cells that divide by budding, germination tubes, real hyphae, and pseudohyphae. The generation of germination tubes is the first stage in the development of true hyphae, and this ability to undergo morphological change has been suggested as a possible pathogenic factor. Human epithelium cells are easier for *Candida albicans* hyphae to penetrate and contact[53].

This shows that rather than growth being fully stopped, morphogenesis is particularly impeded. The fact tea tree oil indicates between environmental stress and blooming growth is more beneficial under these conditions may be related to the prevalence of budded forms. The ability of tea tree oil to prevent

germination tube formation may help to partially explain the reported symptomatic improvement. To sum up, tea tree oil suppresses *Candida albicans* germination tube formation and budding growth at high concentrations[53].

4.3 Frankincense oil

For thousands of years, frankincense oil, which has its roots in India, Africa, and the Middle East, has been valued both economically and socially as an ingredient of incense and perfumes. By tapping Boswellia trees, aromatic solidified gum resins can be obtained, which are then used to make frankincense oil. Boswellic acid, a substance with anti-neoplastic effects, is one of the main ingredients of frankincense oil. *Boswellia carteri* plants yield the highest-quality frankincense resins[18]. In traditional medicine of many nations, the resinous extracts of *B. carteri* and *B. serrata* were historically employed to treat Rheumatoid Arthritis (RA) and other inflammatory disorders including Crohn's disease. One of the most popular oils used in aromatherapy is frankincense oil, a liquid extract made by steam distilling frankincense gum resin[54].

The complex blend of monoterpenoids, sesquiterpenes, and diterpenes found in frankincense essential oil may help explain some of its antifungal properties. Several active components of frankincense oil shown antifungal efficacy against the common fungus Candida albicans. α-pinene, β-pinene, limonene, and β-caryophyllene were some of these ingredients. The most prevalent components in frankincense essential oil were alpha-pinene, beta-pinene, and limonene. These chemicals were principally in charge of the oil's antifungal effectiveness against the common molds like *Aspergillus niger* and *Penicillium chrysogenum*[55].

Uncertainty surrounds the precise approach by which frankincense functions as an antifungal drug. According to some research, frankincense oil and its constituents may prevent the growth of fungi by impairing the integrity of their cell membranes and changing their cellular metabolism[56]. Frankincense oil may prevent the growth of biofilms, a type of protective structure that fungus can create to avoid the immune system and withstand antifungal medications[57]. In addition to its putative antifungal activities, frankincense has also been investigated for its analgesic, anti-inflammatory, and immunomodulatory effects. More research is necessary to completely comprehend the mechanisms of action and therapeutic potential of frankincense for a number of medical disorders[58].

4.4 Lemon oil

The Rutaceae family includes the flowing plant known as lemon (*Citrus limon*). The fresh peels of lemon are used to extract the volatile essential oil known as lemon oil. It is a complex mixture of monoterpenoid, sesquiterpenes, ketones, aldehydes, alcohols, and esters, among other natural substances. Limonene, which accounts for between 50 and 70 per cent of lemon oil's entire makeup, is its main constituent. Several of medicinal qualities are due to the monoterpene limonene, which has a potent citrus scent[59]. By boosting the activity of antioxidant enzymes like superoxide dismutase and catalase, limonene can lower oxidative stress and suppress the generation of inflammatory cytokines like tumor necrosis factor-α and interleukin-1β[60]. Lemon oil's unique lemony scent is derived from a blend of two isomeric aldehydes called citral (neral and geranial). It contains antifungal, antiviral, and antibacterial properties[61]. Citral has the ability to damage the membranes of bacteria and stop the action of vital enzymes including ATPase and gyrase[62]. Lemon oil contains significant amounts of this monoterpene as well. It possesses analgesic and anti-inflammatory qualities[60]. By triggering the opioid system, it can block the synthesis of inflammatory mediators such dinoprostone and nitrogen oxide and lessen pain[60]. An alcohol with a floral, lavender-like fragrance is called linalool. Gamma-aminobutyric acid receptors and their activity, which controls anxiety and stress, can be modulated[63]. It can aid in promoting relaxation and lowering tension because it has hypnotic and anxiolytic qualities[63]. Terpineol is a terpene alcohol with a delightful flowery scent. It possesses antioxidant and antimicrobial qualities. It has the ability to alter the shape and functionality of bacterial and fungal cell membranes and stop the replication of pathogenic organisms[64].

The minor components γ-terpinene, terpinolene, α-pinene, β-bisabolene, and nerol are also found in lemon oil. The scent and medicinal qualities of the oil are also influenced by these components.

4.5 Peppermint oil

The hybrid variety of mint known as peppermint (*Mentha piperita*) is a mixture of spearmint and watermint. The plant, originally from Europe and the

Middle East, is now widely farmed across the world. It occasionally coexists with its parent variety in the wild[65]. Peppermint camphor, Dipentene, Menthone, Apigenol, and Sesquiterpine are active ingredients found in peppermint oil. Peppermint oil contains at least 44 per cent free menthol. Peppermint and menthone, which are both in abundance, are the principal causes of activity[66]. Ingredients are sensitive to the plant's maturity, latitude, and climate[65].

There are two possible pathways for antifungal effects of peppermint. Morphological changes like erratic, flattened, vacant and smooth hyphae as well as some depressions on the outermost layer of cells caused structural changes like a delay in the fungal growth phase's loss of coloration, disrupted chlamydoconidia structure, pit creation, depression of the cell surface, and plasmolysis. The connection with peppermint oil and the plasma membrane of the fungal pathogen was likely what caused the fungi hyphae to leak[66].

5. Conclusion

Onychomycosis is a common fungal infection affecting the nails, and it can be challenging to treat. While there are several conventional treatments available, phytochemicals have been explored as a potential alternative therapy. Studies have investigated the antifungal properties of various phytochemicals, such as tea tree oil, clove oil, frankincense oil, and essential oils. These compounds have shown promising results in laboratory trials for treating onychomycosis. However, further research is needed to determine the optimal concentration, mode of application, and long-term safety and efficacy of phytochemicals for treating onychomycosis. Additionally, it is important to consult with a healthcare professional before using any alternative therapy, especially for a medical condition such as onychomycosis. Overall, phytochemicals have the potential to be an effective treatment for onychomycosis.

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