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# A Review of Herbal Antifungal Drugs: Turmeric, Chamomile, Honey, Neem, and Aloe Vera

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### ABSTRACT

Traditional medicine has harnessed the therapeutic potential of various plant extracts in the treatment of fungal infections, and some of these remedies have undergone in vitro testing for their antifungal properties. This systematic review aims to evaluate the efficacy of antifungal herbal preparations that have been examined in controlled clinical trials. The reviewed treatments exhibit exceptional effectiveness in addressing fungal diseases such as eczema, psoriasis, ringworm, athlete's foot, skin acne, and jock itch, which are caused by various fungal species: Candida albicans for eczema and psoriasis, Trichophyton, Microsporum, and Epidermophyton for ringworm, dermatophytes for athlete's foot and jock itch, and Malassezia yeast for skin acne. Fungal pathogens are responsible for a significant global health burden, contributing to at least 13 million infections and 1.5 million deaths annually. This review delves into the various skin fungal infections, explores potential treatments, and highlights the effective utilization of plant extracts as a promising avenue for combatting these conditions. Medicinal plants with their plant parts are reported to possess antifungal activity. This study evaluated the beneficial effects of the fungal infection.

Keywords: Fungal infection, herbal drugs, Antifungal, Ringworm, athlete's foot, skin acne, jock itch

## INTRODUCTION

The humans live in peaceful coexistence with microorganisms but these microorganisms are capable of creating abnormalities in normal day-to-day human life that is term as infection when the defense system is damaged or the concentration of pathogens reaches to the high density. Bacteria, viruses, parasites, fungi, prions, worms, and helminths have all been involved in causing infectious diseases. A few decades ago, an infection caused by bacteria was the most feared and the strategies to control bacterial infections in patients improved, but nowadays, fungi are the most hazardous pathogens [1]. Fungi exist in two basic forms: Yeasts and molds. Yeasts are typically single, small, and oval cells, whereas mold colonies consist of filamentous strands called hyphae. Some fungi are dimorphic and exist either as yeasts or molds depending on the external environment such as temperature [2,3].

## TOPICAL/SUPERFICIAL DISEASE CAUSED BY FUNGAL PATHOGENS:

Superficial fungal infections occur in the outermost layers of the skin, nails, hair, and mucous membranes [4].

#### Athlete's Foot (Tinea Pedis):

Tinea pedis is a dermatophyte infection of the foot, affecting particularly the toes and sole caused mainly by Trichophyton rubrum, Trichophyton mentagrophytes, and Epidermophyton floccosum pathogens. This infection affects 15–30% of the population [5] and is the most common dermatophyte fungal disease that occurs in man [6]. Individuals with tinea pedis may be susceptible to secondary bacterial infection with, for example, Group A streptococcus [7].

#### **Ringworm (Tinea Corporis):**

Two major causative organisms causing tinea corporis are T. rubrum, T. mentagrophytes affecting neck, trunk, and extremities. The classic tinea corporis lesion is a sharply defined circular lesion with erythema, scaling, and small blisters or pustules at the border. The lesion is usually <5 cm in diameter. The fungus is often transmitted from domestic animals, such as cats, dogs, hamsters, and guinea pigs to humans [5].

#### Jock Itch (Tinea Cruris):

Tinea cruris, also known as jock itch, is an infection involving the genital, pubic, perineal, and perianal skin caused by pathogenic fungi known as dermatophytes [8][9][10][11]. These dermatophytes affect keratinized structures such as hair and the epidermis' stratum corneum resulting in a

characteristic rash. Intertriginous areas are hospitable environments for fungus, with sweating, maceration, and alkaline pH being responsible for the groin's predilection for infection [8][10][11][12].

#### **Dermatophytosis:**

Dermatophyte fungi are organisms that digest keratin [13].Dermatophytes infect the stratum corneum of the epidermis and keratinized tissues derived from it, such as hair or nail. Trichophyton spp., Microsporum spp., and Epidermophyton spp. are responsible for most of the superficial fungal infections, although the causative agents can be some yeast and some non dermatophyte molds [14].

**Tinea Capitis:** The predominant causative agent of this infection is Trichophyton tonsurans and mainly causes disease in childhood, presenting with alopecia and scaling on the scalp [15,16].

#### Tinea unguium or onychomycosis (nails):

T. rubrum and T. mentagrophytes dermatophytes are the principal causes of onychomycosis, accounting approximately for 90% of toenail infections and 50% of fingernail infections [17-19].

#### Superficial candidiasis:

Superficial candidiasis infections are usually caused by Candida albicans, and this organism is a common commensal in the mouth, vagina, and gastrointestinal tract in healthy individuals. The prevalence of carriage is greater in hospitalized patients and those who are immunocompromised.

#### Candidiasis of the skin:

Candidiasis of the skin is often confined to body folds, including the inter-digital spaces of the hands or feet. Typically, small satellite pustules lie distal to the periphery of the rim of the rash. Chronic paronychia (nail fold infections) can be caused by Candida.

## **Drug Information:**

#### 1. Turmeric oil



Scientific name: Curcuma longa.

Synonym: Haldi, Curcuma longa, Haridra, Indian saffron.

Biological Source: Turmeric consist of the dried rhizome of Curcuma domestica (Curcuma longa)., belonging to Family Zingiberaceae., Kingdom plantae.

Geographical source: the drug is cultivated in topical Asia and Africa especially in India, west Pakistan, China and Malaya.

**Morphology:** The primary rhizomes are ovate or pear-shaped, oblong or pyriform or cylindrical, and often short branched. The rhizomes are known as 'bulb' or 'round' turmeric. The secondary, more cylindrical, lateral branched, tapering on both ends, rhizomes are 4–7 cm long and 1–1.5 cm wide and called as 'fingers. The bulbous and finger-shaped parts are separated and the long fingers are broken into convenient bits. They are freed from adhering dirt and fibrous roots and subjected to curing and polishing process. The curing consists of cooking the rhizomes along with few leaves in water until they become soft. The cooked rhizomes are cooled, dried in open air with intermittent turning over, and rubbed on a rough surface. Colour is deep yellow to orange, with root scar and encircling ridge-like rings or annulations, the latter from the scar of leaf base. Fracture is horny and the cut surface is waxy and resinous in appearance. Outer surface is deep yellow to brown and longitudinally wrinkled. Taste is aromatic, pungent and bitter; odour is distinct [20].

**Chemical constituent:** Medicinal uses of the rhizomes arise from volatile oil as a carminative and antifungal activity and yellow curcuminoids for antioxidative and anti-inflammatory properties. Active constituents in turmeric volatile oil are turmerone, atlantone, and zingiberone [21, 22]. Turmeric oil isolated from turmeric rhizome possesses effective antifungal activity against dermatophytes [23, 24]. The creams containing 3–8% w/w turmeric oil showed similar antidermatophytic activity [25].

#### Uses:

- Curcumin and turmeric oil exert antifungal effect against two phytophagous fungi, namely, *Fusarium solani* and *Helminthosporium oryzae*. Turmeric oil exhibited the most effective antifungal activity against *F. solani* and *H. oryzae* with IC<sub>50</sub> of 19.73 and 12.7 μg/mL, respectively [26].
- Turmeric oil possesses good antioxidant, antimicrobial, anticancer, anti-hyperlipidemic anti-inflammatory, anti-diabetic, and hepato-protective properties [27].
- 3) Apart from medicinal fields, this oil has also a great future in the cosmetics, pesticide, and food industries due to its rich chemical profile [27].
- 4) several studies have shown that C. longa and its bioactive compounds possess numerous pharmacological activities such as antioxidant, hepatoprotective, anti-osteoarthritis, anti-inflammatory, anticancer, anti-arthritic, neuroprotective, antidiabetic, antidiarrheal activity, anti-microbial, anti-atherosclerotic, antidepressant, anti-ageing, wound healing and memory enhancing activities.

#### 2. Chamomile oil



Scientific name: Matricaria chamomilla L.

Synonym: Chamomilla, Chamomilla recutita, Matricaria chamomilla, and Matricaria suaveolens.

Biological Source: This consist of dried flower heads of chamomilla-reticulate or mantricaria reticulate family (compositae) Asteraecae.

Geographical source: Chamomile is an annual or perennial plant native to temperate regions of Asia and Europe. It is widely cultivated worldwide, such as in Germany, Hungary, France, Russia, Brazil and western Xinjiang of China.

**Morphology:** This plant is native to tropical conditions but it can be cultivated in cold climatic conditions [28]. The roots are thin, spindle-shaped and grow straight. The stems can grow to 10–80 cm. The leaves are long, narrow and pinnate, with fissures. The head is about 10–30 mm in diameter [29, 30]. Matricaria chamomilia L. has small white flowers of the Compositae family and, at their centre, a yellow tubular petal is present. Anthemis nobilis (L.) All. contains flowers with double petals, soft stems, and has a green apple fragrance. It is also called "the apple of the ground". In addition, it is also known as the "Physician of Plants" due to its ability to heal sick plants around it. Although MC and CN are similar in appearance, they have distinct differences. The petals of MC are turned down and have a raised conical center, whereas the center of CN is flat [31].

**Chemical constituent:** Two most prominent compounds found in oils of M. chamomilla, farnesol and  $\alpha$ -bisabolol, have potential antifungal activity [32].  $\beta$ -farnesene,  $\alpha$ -farnesene, and  $\alpha$ -bisabolol and its oxide were reported as its main compounds [33, 34]. Essential oils with these were observed to have good antifungal activity against A. niger, Aspergillus sp. and Candida albicans [35]. The investigation in Estonia on the essential oil of chamomille (M. recutita) indicated that the main constituents of the essential oils were as follows: bisabolol oxide A (39.4%), bisabolone oxide A (13.9%), (Z)-en-yndicycloether (11.5%), bisabolol oxide B (9.9%),  $\alpha$ -bisabolol (5.6%), and chamazulene (4.7%) [36]. Chamomile contains flavonoids, coumarins, volatile oils, terpenes, sterols, organic acids, and polysaccharides, among other compounds. Having a wide array of compounds

#### Uses:

- a natural peptide from the plant, has broad-spectrum antifungal activity against human pathogenic moulds and yeasts. It kills Candida albicans by increasing cell membrane permeability and inducing reactive oxygen species (ROS) production [38]
- chamomile exhibits various pharmacological activities such as anticancer, anti-inflective, anti-inflammatory, antioxidant, hypoglycaemic, hypotensive, hypolipidaemic, antiallergic, antidepressant, and neuroprotective effects, and others.

#### 3. Honey



Scientific name: Apis

Synonyms: Madhu, Honey Purified, Mel.

**Biological source:** Honey is a sugar secretion deposited in honey comb by the bees, Apis mellifera, Apis dorsata and other species of Apis, belonging to family Apidae, order Hymenoptera.

Geographical source: Honey is available in abundance in Africa, India, Jamaica, Australia, California, Chili, Great Britain and New Zealand.

**Morphology:** Colour: Pale yellow to reddish brown viscid fluid, Odour: Pleasant and Characteristic, Taste: Sweet, slightly acrid, Extra: Features However, the taste and odour of honey solely depends upon the availability of surrounding flowers from which nectar is collected. On prolonged storage it usually turns opaque and granular due to crystallization of dextrose and is termed as 'Granulated honey'

**Chemical constituents:** Hydrogen peroxide is the major contributor to the antimicrobial activity of honey, and the different concentrations of this compound in different honeys result in their varying antimicrobial effects [38- 41]. However, generally honey has a content of 80–85% carbohydrates, 15–17% water, 0.3% proteins, 0.2% ashes and minor quantities of amino-acids, phenols, pigments and vitamins [42-43]. Beside these other components are also found in minor concentration.

#### Uses:

1) Several studies have investigated the antimicrobial properties of honey against bacteria, few have focused on its antifungal properties [44].

2) The antifungal properties of honey make it an attractive alternative treatment for Candida-associated infections, particularly for topical application to the skin and mucous membranes [45].

3) Honey appears to heal partial thickness burns more quickly than conventional treatment (which included polyurethane film, paraffin gauze, soframycinimpregnated gauze, sterile linen and leaving the burns exposed) and infected post-operative wounds more quickly than antiseptics and gauze.

#### 4. Neem oil



Scientific name: Azadirachta indica

Synonym: Neem, Margosa, Azadirachta.

**Biological source:** Neem consist of almost all parts of the plants which are used as drug some importance morphology parts are the dried stem bark, root bark, leaves and fruits of azadirachtaindica also, known as Melia azadirachta, family Meliaceae.

Geographical source: It is found in India, Pakistan, Sri Lanka, Malaya, Indonesia, Japan, tropical region of Australia and Africa. in India, it is found in uttar Pradesh, Maharashtra, Tamil Nadu, Rajasthan, and M.P.

**Morphology:** Neem tree belongs to the family Meliaceae which is found in abundance in tropical and semitropical regions like India, Bangladesh, Pakistan, and Nepal. It is a fast-growing tree with 20–23 m tall and trunk is straight and has a diameter around 4-5 ft. The leaves are compound, imparipinnate, with each comprising 5–15 leaflets. Its fruits are green drupes which turn golden yellow on ripening in the months of June–August [46].

**Chemical constituents:** The most important active constituent is azadirachtin and the others are nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinate, gedunin, salannin, and quercetin. Leaves contain ingredients such as nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7-benzoylazadiradione, 7-desacetyl-7-benzoylgedunin, 17-hydroxyazadiradione, and nimbiol [47,48]. Quercetin and β-sitosterol, polyphenolic flavonoids, were purified from neem fresh leaves and were known to have antibacterial and antifungal properties [49] and seeds hold valuable constituents including gedunin and azadirachtin.

#### Uses:

1) Leaf and seed extracts of *A. indica* were tested for antidermatophytic activity and found effective against some dermatophytes such as *Trichophyton rubrum*, *T. violaceaum*, *Microsporum nanum* and *Epidermophyton floccosum* by the tube dilution technique [50] and on *C. albicans* [51].

2) Neem leaf and its constituents have been demonstrated to exhibit immunomodulatory, anti-inflammatory, antihyperglycaemic, antiulcer, antimalarial, antifungal, antibacterial, antioxidant, antimutagenic and anticarcinogenic properties[52].

#### 5. Aloe vera



#### Scientific name: Aloe Vera

Synonyms: The species has several synonyms: Aloe barbadensis Mill., Aloe indica Royle, Aloe perfoliata L. var. vera and Aloe vulgaris Lam.

**Biological source:** The biological source of aloe is dried latex of leaves of it. It is also known as curacao aloe, cape aloe and socotrine aloe. It belongs to the liliaceae family.

**Geographical sources:** Aloe species are mostly inhabitants of arid climates, and are widely distributed in Africa, India, and other arid areas. The largest number of Aloe species is approximately 140, and most are found in South Africa However, they could also be grown in subtropical summer rainfall and winter rainfall regions the species requires well-drained, sandy potting soil, and bright, sunny conditions.

#### Morphology:

Aloe vera is a spiky cactus like xerophytes. It is a clump forming perennial plant with thick fibrous root which produces large basal leaves, usually 12–16 per plant, weighing up to 1.5 kg when mature. The plant matures when it is about 4 years old and has a life span of about 12 years. The leaves are up to 0.5 m long and 8–10 cm across at the base, tapering to a point, with saw-like teeth along their margins. In a transverse section, the plant shows a slightly concave appearance on the adaxial surface and distinctly convex appearance on the lower abaxial surface [53]. The leaves are covered with thick cuticle, beneath which epidermis and mesophyll are present. Later is differentiated in upper chlorenchyma and lower parenchyma, as the rosette mature, successive leaves have fewer whitish spots and grey-greenish in color [54]. The plant can be harvested every 6–8 weeks by removing 3–4 leaves per plant. Red, yellow, purple or pale stripped flowers are present most of the year growing in a long raceme at the top of the flower stalk which originates from the centre of the basal leaves. The flower stalk grows up to 1.5 m in height. The fruit is a triangular capsule containing numerous seeds. The plant is practically disease free, occasionally black spots may occur on upper surface because of fungal infection or soft rottening may damage whole plant. The causal organism for soft rottening is a bacterium. Frost is another enemy of aloe vera plant and it cannot survive in frost conditions [53]. There are over 550 species of aloe grown world over. However, only two species are grown commercially i.e. Aloe barbadensis Miller (Aloe vera) and Aloe aborescens Miller. There are at least two other species that have medicinal properties namely Aloe perry baker and Aloe ferox. Most aloe vera plants are non toxic but a few are extremely poisonous containing a hemlock like substance (55).

**Chemical constituent:** Aloe vera contains 6 antiseptic agents: Lupeol, salicylic acid, urea nitrogen, cinnamonic acid, phenols and sulfur. They all have inhibitory action on fungi, bacteria and viruses. Aloe vera inhibits the cyclooxygenase pathway and reduces prostaglandin E2 production from arachidonic acid. Recently, the novel anti-inflammatory compound called C-glucosyl chromone was isolated from gel extracts [56]. An increased synthesis of hyaluronic acid and dermatan sulfate in the granulation tissue of a healing wound following oral or topical treatment has been reported [57]. Glucomannan, a mannose-rich polysaccharide, and gibberellin, a growth hormone, interacts with growth factor receptors on the fibroblast, thereby stimulating its activity and proliferation, which in turn significantly increases collagen synthesis after topical and oral Aloe vera [58]. The most important constituent of aloe are the three isomers of Aloens, Barbaloin,  $\beta$ -Barboloin and Isobarbolin.

1) Aloe vera gel has been reported to have a protective effect against radiation damage to the skin [59,60].

2) Its moisturizing effects has also been studied in the treatment of dry skin associated with occupational exposure where aloe vera gel gloves improve the skin integrity, decreases the appearance of fine wrinkle, and decreases erythema [61].

3) It also has an anti-acne effect.

## **Result and Discussion**

Most of the plants exhibit anti-fungal and anti-infective effects in animals as well as in humans, which may be helpful in fungal infections and their associates. Different parts of the plant contain a profile of important phytochemical constituents that are mostly responsible for its biological action. Different parts of plants (leaf, seed, bark, and root) possess antifungal properties. Polar and non-polar solvents are used for the extraction of various parts of plants. The result revealed that the aqueous and ethanol extract of most of the parts contain Azoles, alkaloids, tannins, flavonoids, anthraquinone, and carbohydrates which have been discussed in this study. These herbs can be better than other available sources. because there are no uniform known toxic effects of these in therapeutic dosage while they are traditionally been used since ancient times.

#### Conclusion

The current review discussed the chemical constituents, pharmacological effects and therapeutic importance promising medicinal plant with wide range of pharmacological activities which could be utilized in several medical applications because of its effectiveness and safety. in people with weakened immune systems, these fungi are more likely to cause an infection. And is increased rapidly in developing countries like India. The disease related complications were increasing rapidly even if there are available of treatment with standard drugs. Plant medicines were traditionally used and they were less toxic with no side effects. The ability of the plant extracts was due to the capacity to restore Azoles prevent the fungal cell wall to form sterol (ergosterol) by obstructing the oxidative enzymes of the fungal cell membrane. This leads to incomplete synthesis and enhanced permeability of the fungal cell wall. characterize the plant medicated compound with novel mode of mechanism to control and manage fungal infection as the disease.

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