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Dermatophytes and ringworm infection

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Abstract

For both people and animals, superficial fungal infections affecting the keratinized layers of skin and its appendages are usually referred to as "ringworm." All layers of the skin can be penetrated by ringworm fungi, or dermatophytes, although they are usually limited to cornified areas of the skin “stratum corneum”. Dermatophytosis is the name for a medical condition caused by dermatophytes. Virtually, there is no human population free from these mycotic diseases and about 25% of the world population are infected by derrmatophytosis. Three genera, *Microsporum*, *Epidermophyton,* and *Trichophyton* (Fungi Imperfecti) in Hyphomycetes, the anamorphic class of the Deuteromycota, are the causative agents of dermatophytosis. *Trichophyton rubrum* appears to be the most common causative agent of ringworm infections, followed by *Trichophyton interdigitale* and *Microsporum canis.* It is critical to advance our understanding of fungal biology and pathology and to raise public awareness of the importance of these infections by providing accurate epidemiological data. Ecological groupings, pathogenic potential, clinical manifestation and therapy “chemical and natural” for dermatophytosis are reviewed.

Keywords: Dermatophytosis; Keratinophilic; Plant; Tinea; Therapy

1. Introduction

A class of molds with similar physiological characteristics is called dermatophytes, and some of them can cause particular medical condition which is dermatophytoses (ringworm, tineas). They are possessing the ability to attack cornified tissue of human and other animals result in scaly skine, broken hairs and crumbling nails. Because the fungi are unable to enter the mucosal surfaces, deeper tissues, or organs of immune-competent hosts, this infection is limited to the cornified layers. Two key characteristics of dermatophytes are there, keratinophilic and keratinolytic activities. This indicates that they may break down keratin in its saprophytic condition *in vitro* and use it as a substrate. Additionally, some of them have the potential to infiltrate tissues *in vivo* and cause tineas [1, 2].

In general, dermatophytes can be divided into three types according to the habitat in which they live. Only seldom are geophilic species—soil-dwelling saprophytes—that are pathogenic to humans or other animals. Animals are the typical hosts of zoophilic organisms, although they can also infect humans. These are believed to have transformed into keratinophilic fungi, which parasitized animal hosts, after acquiring how to hydrolyze keratinous detritus found in the soil. Restricted to humans as hosts, anthropophilic organisms are thought to have developed from zoophilic fungus. It is possible for diseases to spread from one human to another, from one animal to another, and from soil to either humans or animals [3].

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2. Taxonomy of Dermatophytes

Dermatophytes have been routinely placed in the class Deuteromycetes or "Imperfect Fungi". The dermatophytes' sexual state is helpful for epidemiological research and for identifying particular species. Thus, dermatophyte species can be divided into three genera according to variations in conidial morphology: *Microsporum, Epidermophyton,* and *Trichophyton* [4].

2.1. Epidermophyton

Large, multicellular, club-shaped, thin-walled macroconidia that are grouped in bunches define this genus; microconidia are not generated. Features of the genus are derived from *E. floccosum*. There are two species of *Epidermophyton* based on anamorph morphology, (*E. floccosum* and *E. stockdaleae*). *E. floccosum* is the only pathogenic ''anthropophilic'' species in this genus that is found globally responsible for the majority of tinea cruris infections [5].

2.2. Microsporum

There are microconidia and macroconidia in this genus. Macroconidia are spindle-shaped, multiseptate, and have a thin or thick echinulate cell wall. They can also be abundant or rare. However, the echinulations on the macroconidial cell wall serve as this genus' primary characteristic that sets it apart. Pyriform microconidia measure roughly 2-3 µm. *M. audouinii* is the type species. On the basis of anamorph morphology, there are approximately 18 species of *Microsporum*. In the Mediterranean region, tinea corporis and tinea capitis are most frequently caused by *M. canis* [6].

2.3. Trichophyton

This genus produces microconidia “2-3 µm pear-shaped” and macroconidia “cigar-shaped” with smooth walls. Based on anamorph shape, *Trichophyton* is divided into 25 species and *T. tonsurans* is the type species [6, 7]. In Central and North Europe, *T. rubrum* is the most prevalent dermatophyte within the past 20–30 years. According to reports, in the United States and Canada, the most commonly isolated organism in infecting children with tinea capitis is *Trichophyton tonsurans*, while the isolated organism in tinea pedis and tinea cruris is *T. mentagrophytes* var. *interdigitale,* a member of the *T. mentagrophytes* [8, 9].

3. Pathogenic potential of dermatophytes

The ability to utilize the host environment as a growth medium and to overcome the host's defense mechanisms is known as pathogenicity [10]. Dermatophytes are provided with an arsenal of proteases “keratinases” which allows them to invade tissues like the stratum corneum and intended to break down the keratin network into assailable amino acids or oligo-peptides. Fungi benefit from self-synthesized enzymes in a variety of ways. They improve survival in tissues by physically or chemically altering the immediate environment, and they operate directly through the breakdown of host proteins, giving a source of nourishment. As a result, a fungal agent's pathogenic potential is determined by its ability to synthesize enzymes. Variations in a fungus's enzymatic potential, in turn, may be responsible for changes in the pathogenic consequences of different strains [11, 12].

Keratin, collagen, and elastin constitute approximately 25% of mammalian body weight. Enzymes which released from the mycelium have the ability to break down keratin and associated fibrous proteins from the skin, nails, and hair. The soluble proteins, peptides, and amino acids released from these substrates along with changes in the environment's pH, changes in the structure of hairs, or a decrease in their weight are typically used to estimate the keratinolytic activity [13, 14].

The abundance of glycoproteins containing mannans in the cell walls of dermatophytes has been linked to their ability to stick to cell surfaces; the greater their adhesion capability, the greater their pathogenicity and ability to invade host cells. The hyphae must pierce the skin of the body and the arthroconidia must germinate quickly for dermatophytes to successfully establish themselves in their host; otherwise, the epithelium will continue to shed its cells. [15, 16, 17].

Plate assays, diagnostic kits, and liquid media were used to demonstrate the synthesis of lipases, glycosidases, phosphatases, and amylases in dermatophytes. In addition to media containing lipids, keratin-containing media and even sabouraud glucose-peptone broth (phospholipase A) can yield lipases and phospholipases. Arthroconidia germinate when there is high humidity and the stratum corneum provides nutrients. This likely explains why warm, moist conditions is associated with a higher risk of fungal skin infections. The germination rate of *T. mentagrophytes* conidia was significantly increased by activating them for 24 hours at 25°C in distilled water [18, 19].

4. Clinical Manifestation

Traditionally, dermatophytosis have been termed for the anatomical parts involved by attaching the Latin term referring to the body site following the term tinea [20].

4.1. *Tinea Corporis* (glabrous skin)

It requently affecting the shoulders, limbs, or trunk; the face is also occasionally affected. The infection can be moderate or severe, and it typically manifests as annular, scaly spots or plaque with central clearing and an elevated, scaling border. When zoophilic dermatophytes produce chronic infections, it might manifest as papules and vesicles along with dermal infiltrates [21]. The distribution and causative agent for tinea corporis varied from a locality to another and based on where the infection originated. Since *T. rubrum* spreads from the foot of those who have tinea pedis, it is most likely the most frequent cause globally. The most frequent cause of tinea capitis, *T. tonsurans*, is also the source of tinea corporis in regions where tinea capitis is widespread. If the spread originates from a pet, *M. canis* is typically the culprit. *T. verrucosum, E. floccosum*, *T. mentagrophytes,* and *M. audouinii* are some other dermatophytes that cause problems [21, 22].

4.2. *Tinea Barbae* (beard and mustache)

Tinea of the chin and upper lip is referred to as tinea faciei. Lesions are three types: deep inflammatory plaques, non-inflammatory superficial areas, and severe pustular eruption. Endothrix invasion in the affected area might result in brittle, lusterless hair [23]. The ultimate result could be significant scarring and permanent hair loss, *T. verrucosum* and *T. mentagrophytes* var. *granulosum*, are more frequently causative agents Diseases are acquired through contact with cattle, dogs, and other animals; thus, dairy producers and cattle ranchers are commonly affected. Person-to-person transmission can occur in barbershops where antiseptic methods are not employed. Omran *et al.* (2008) stated that *T. mentagrophytes* was most prevalent agent of positive culture of tinea barbae [24, 25].

4.3. Tinea Imbricata

A particular form of tinea corporis, is dispersed through the body and affects people of all ages. Geographically, it is limited to some of the islands in the Pacific Ocean, Southeast Asia, Mexico, Central America, and South America. The only known etiologic agent is *T. concentricum*, a dermatophyte that is exclusively anthropophilic [15, 26].

4.4. *Tinea Cruris* (Jock Itch) (groin)

It is usually more common in young adults. Nonetheless, post-pubertal females who are overweight or who frequently wear tight pants are more likely to be affected. Although the clinical presentation of tinea cruris varies, the background rash is red to reddish-brown, acute rashes also may have a burning quality. Chakrabarti *et al.,* (1992) studied 60 individuals who have a medical suspicion of tinea cruris and found that the most causative agents were *T. rubrum* [27, 28, 29].

4.5. *Tinea Capitis* (lashes, eyebrows, and scalp)

It is one of the most frequent forms of dermatomycosis. Less than 5% of tinea capitis infections in the USA are brought on by *Microsporum* species, while more than 90% of cases are due to *T. tonsurans*. These two species penetrate hair shafts and go beyond surface inflammation. The infection may be minor, almost subclinical, with patchy areas of scaling and pale gray hair stumps along with mild erythema, or it may be severe, resulting in kerion and folliculitis development. Three terms that can be used to describe an infection of the hair are favus, endothrix, and ectothrix, which refer to the sheath of arthroconidia that forms inside the hair shaft and outside the hair shaft, respectively, while black dot is left behind when infected hairs abruptly break off at the follicular opening [30]. Moore (1993) found that *T. tonsurans* was the causative agent in cases of tinea capitis, followed by *M. canis* and *M. audouinii. T. mentagrophytes* var. *granulare, M. gypseum*, while *T. rubrum* was less common isolates [31, 32]. Seebacher *et al.*, (2008) reported that, *T. mentagrophytes* var*. granulare* and *M. canis* were the most common dermatophytes, followed by *E. floccosum, T. tonsurans, M. nanum, T. violaceum,* and *T. concentricum*. *T. violaceum* is endemic among the 824 kids enrolled in a school in Ethiopia [33]. Aktas *et al.*, (2009) reported that the most common agent was *M. canis,* followed by *T. tonsurans, M. audouinii,* and *T. verrucosum* in tinea capitis between 2006 and 2008 in 48 children in Erzurum, Turkey [34].

4.6. *Tinea Pedis* (Athlete's Foot)

Men are more likely than women to contract this fungal infection, which generally affects men between the ages of 20 and 40. This infection usually starting in the interdigital clefts then spreads to ankles, dorsum, soles, legs, and toenails, a condition known as tinea unguium. Patients with diabetes are thought to have a 50% increased risk of developing a

fungal infection, such as tinea pedis [35]. Tinea pedis is differentiated into interdigital type, squamous-hyperkeratotic type and vesiculous-dyshidrotic type. The most prevalent clinical manifestation is the interdigital, which mostly affects the gaps between the fourth and fifth toes and manifests as maceration, fissuring and peeling. Squamous-hyperkeratotic type (hyperkeratosis and acanthosis) where the pinkish skin of the heels, sides, and soles of the foot is covered in tiny silvery scales (moccasin foot), and vesiculous-dyshidrotic type. The etiology of the complex infection, which is a combination dermatophyte and bacterial infection, is polymicrobial infection and is clinically more severe [36]. Melikoğlu *et al.*, (2023) stated that the dermatophyte that cause tinea pedis were identified as *T. rubrum, T. mentagrophytes, M. Canis, E. Floccosum, T. verrucosum* and *T.violaceum* with decreasing frequency [37].

4.7. Tinea Unguium

About 20 percent of nail diseases are caused by onychomycosis. Mostly, 80 – 90%, *T. rubrum* and *T. mentagrophytes* var. *interdigitale* are the most common causative agents of tinea unguium. Children's nails develop faster and have smaller surfaces than adults, so that nfection rates in children are thirty times lower than in adults [38]. Vestergaard-Jensen *et al.*, (2022) reported that the common dermatophyte species that was isolated from nails of the feet in 1,305 children between the ages 3 and 15 in 17 schools were *T. tonsurans*, *T. rubrum*, and *T. mentagrophytes* [39].

4.8. Tinea Versicolor

It is known as pityriasis versicolor, is caused by lipophilic dimorphic fungi that are members of the *Malassezia* genus. (*Pityrosporum ovale* or *Pityrosporuni orbiculare*) which are included in the normal skin flora. Usually, it appears as tiny to medium-sized erythematous, hyper- or hypopigmented macules that are round or oval in shape. Usually, delicate desquamation covers the upper part of the trunk, particularly shoulders, neck, and, sometimes, the face. Fungal proliferation can occur in filamentous and yeast structures due to several circumstances, including the use of oily lotions, humidity, the abuse of corticosteroids, or genetic traits [40].

4.9. Tinea Manuum

T. rubrum, the most common dermatophyte that causes ringworm of the palms of the hands. Diffuse dry scaling lesions that highlight the flexural creases of the palms are often the clinical manifestation of *Tinea manuum*. When additional dermatophytes are implicated, inflammatory lesions are less common but can still result in a persistent reaction [41].

5. Therapy for Dermatophytosis

5.1. Chemical Antifungal Drugs

Itraconazole, miconazole, bifonazole, clotrimazole, ketoconazole voriconazole, and fluconazole are examples of azole derivatives with antifungal properties. These derivatives work by inhibiting a cytochrome (CYP) P450 that is involved in the biosynthesis of ergosterol, which is a crucial part of the fungal plasma membrane. As a key component of secretory vesicles, ergosterol controls membrane permeability and the actions of membrane-bound enzymes. It also plays a significant part in energy production within mitochondria. Currently, severe and chronic dermatophytoses are treated with these systemic medications. However, topical antifungal therapy based on imidazole such as clotrimazole, ketoconazole and miconazole are the most commonly used [42].

5.2. Natural antifungal drugs

The increase in human mycosis leads to the continuous search and discovery of novel antifungal drugs, particularly those derived from natural sources. Methodical studies of higher plants and their volatile oils have produced novel structural models for antifungal medications. Because plants have an inherent defense mechanism against fungus-causing diseases, a great deal of interest has been placed on plant-derived fungicides. Sensing potential phytopathogens, plants can defend themselves against biotic attack by producing antifungal substances which may be necessary for resistance to fungal infections.

Numerous plants have been used traditionally to treat fungal infections, and studying these plants may help develop medications that are effective against harmful fungus that affect humans. Several investigators were interested in making survey and studied the effect of different plant extracts on various pathogens *in vivo* as well as *in vitro*. Steinmetz *et al.* (1995) studied 38 Polyporaceae species' antifungal efficacy against yeasts and dermatophytes using agar dilution technique *in vitro*. The most effective species against pathogenic dermatophytes was *Pycnoporellus fulgens*, which also exhibited broad-spectrum antifungal action against yeasts, including *Candida albicans, Candida glabrata,* and dermatophytes, including *M. canis, M. gypseum, T. mentagrophytes, T. rubrum, and E. floccosum* [43, 44]. Redondo-Blanco *et al.,* (2020) reported that several plants which are widely available in India have antifungal properties, such *Syzygium*

cuminii, Punica granatum, Emblica officinalis, *Terminalia chebula, Delonix regia*, *Pisdium guajava*, *Eucalyptus sp.* and *Caesalpinia digyna* [45]. Bahadar *et al.,* (2016) found that essential oil of *Eucalyptus citriodora* was effective as an antifungal against *T. mentagrophytes, T. rubrum* and *M. nanum.* They found that *M. nanum* was killed in 20 seconds by the pure oil and *T. mentagrophytes* and *T. rubrum* in 15 seconds. The oil concentrations up to 5% showed no side effects when applied to mammalian skin [46]. Uma *et al.,* (2017) stated that *T. rubrum, T. soudanens,* and *T. erinacei* that cause severe mycoses were inhibited by essential oils of *Allium sativum*, *A. fistulosum,* and *A. cepa* [47]. Zuzarte *et al*., (2021) reported that *T. rubrum, M. canis, T. mentagrophytes,* and *M. gypseum* were all markedly suppressed by the hydro-alcoholic leaves extract of *Piper regnellii* [48]. Anand *et al.*, (2022) reported that in Tamil Nadu, ringworm infections are commonly treated using traditional medicines such as *Punica granatum, Cassia alata, Thespesia populnea, Lawsonia inermis,* and *Acalypha indica. Wrightia tinctoria* leaf chloroform extract was active against *T. rubrum, E. floccosum,* and *Aspergillus niger* at 0.5 mg/ml. The primary recognized phytochemical constituent was Indirubin which shown efficacy against *T. rubrum* (MIC = 25 µg/ml), *E. floccosum* (MIC = 6.25 µg/ml), *T. simii* and *T. mentagrophytes* (MIC = 50 µg/ml) [49].

6. Conclusion

Dermatophyes have consistently been one of humanity's parasitic companions and considered as the primary cause of cutaneous disorders. Due to their attraction to keratin, dermatophytes target keratinized tissues like nail, hair, and stratum corneum, resulting in dermatophytosis. With obvious significance to the emerging immunological viewpoints, the area of dermatophytosis immunology is one that is always evolving. The field of skin immunobiology presents numerous opportunities to further our comprehension of disease mechanisms, with dermatophytes serving as a prime example of cutaneous infections that are adapted to their environment but typically under control. Utilizing plant-based solutions to combat fungal infections has garnered a lot of interest in recent years. This is due to the numerous benefits of using medicinal herbs, including lower expenses and fewer adverse effects.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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