KAVAKA 47 : 83 -94 (2016)

Mycokeratinophiles: Pathogens of Onychomycosis

Sandeep Kotwal and Geeta Sumbali
Department of Botany, University of Jammu, Jammu, 180006
Corresponding author Email: geetasumbalippl@yahoo.co.in
(Submitted on July 25, 2016; Accepted on September 20, 2016)

ABSTRACT

Mycokeratinophiles are an ecologically important group of microorganisms that have the ability to cycle keratin, which is one of the most abundant and highly stable animal protein on the earth. These are vigorous and self- sufficient saprophytes as long as environmental conditions are favourable. However, they are opportunists and may become parasitic by accident. After becoming pathogenic, they are able to survive and multiply at host's body temperature, causing further infection by invading fresh keratinized tissues. Infection is transmitted from human to human or from animal to human by direct contact or by contact with infected hairs or epidermal cells. Infact, it is the only type of fungal infection known to be of contagious type. Such mycokeratinophiles, which cause diseases of skin, hair and nails in man and animals, are commonly called as dermatophytes and their infections are known as cutaneous mycoses or dermatomycoses. The dermatophytic fungi belong to one of the three genera- *Microsporum*, *Trichophyton* or *Epidermophyton*. In addition to the dermatophytes, some non-dermatophytic mycokeratinophiles are emerging as leading cause of onychomycosis, that is, fungal infection of toe nails and finger nails. It is the most common nail disorder present in 2-13 per cent of general population, increasing up to 48 percent by 70 years of age. Although onychomycosis is rarely life threatening, its high incidence, prevalence and associated morbidity, makes it an important public health problem.

Key Words: Mycokeratinophiles, mycoses, onychomycosis, dermatophytes, non-dermatophytes.

INTRODUCTION

Mycokeratinophiles are an ecologically important group of microorganisms that have attracted the attention of researchers chiefly because they play an important role in the decomposition of keratin substrates and could be pathogenic to animals, including human beings causing mycosis. Secondly, since mycokeratinophiles are active producers of extracellular keratinases, they can be used in bioremediation of such wastes and waste contaminated sites. For example, several million tonnes of feather waste is generated by poultry and other livestock, which otherwise adds to environmental pollution can be converted into feather meal by using the keratinophilic/ keratinolytic fungi (Shih, 1993; Bertach and Coello, 2005). Addition of feather meal to the animal feed improves digestibility, results in bolstered growth of the poultry and can also be used as slow nitrogen releasing fertilizers (Kushwaha and Gupta, 2008). Keratinases produced by these fungi can be utilized in enzyme-based detergents, cleaning up of clogged drains, leather industry for dehairing, modification of silk and wool fibres, treatment of acne and psoriasis, additives in skin-lightening agents (Kushwaha and Gupta, 2008). Keratinases have also been found to degrade prion protein, leading to the cure of mad cow disease (Shih and Wang, 2006; Wang *et al.*, 2007).

Distribution and abundance

Soil is the natural reservoir of mycokeratinophiles. Their presence and distribution in the soil depends largely on the amount of keratinic material available due to the activities of man or his domestic animals or the wild animals (Mercantini *et al.*, 1983). Other ecological and environmental factors, such as pH, temperature, humidity, soil profile, soil texture and structure also play an important role in their abundance and distribution (Chmel *et al.*, 1972; Vollekova, 1984). In addition, their existence in the soil may also be influenced by the presence of other microbes, namely the bacteria and other fungal species, which may exert antagonistic effects (Srivastava *et al.*, 1990). Reports on the presence of these fungi in different soil habitats of various countries indicate that they are worldwide in distribution. The first report of a mycokeratinophile growing saprophytically in nature was that of Szathmary (1936), who isolated *Trichophyton primum* (*T. gypseum*) from the mud watercourses in the park of the University of Peco. Later, Emmons (1942) demonstrated that soil surveying is an excellent method for discovering the natural habitats of the fungi that are capable of causing human and animal diseases. In 1952, Vanbreuseghem introduced the hair-bait technique, which has been of immense help in the selective isolation of mycokeratinophiles from soil. Since then, this important group of microbes have attracted the interest of mycologists throughout the world (Marchisio, 2000).

A survey of literature reveals presence of keratinophilic fungi in the soil of different countries like United States (Daniels, 1954; Rippon and Medenica, 1964; Baxter, 1966, 1969), Australia and New Guinea (Duries and Frey, 1955), New Zealand and Polynsian Island (Marples, 1965), Japan (Kominami, 1961), Canada (Carmichael, 1962; Padhye *et al.*, 1973; Currah *et al.*, 1996), Czechoslovakia (Otsenasek and Dvorak, 1964; Repova, 1990), Egypt (Taylor *et al.*, 1964; Abdel- Fattah *et al.*, 1982; Youssef *et al.*, 1992), Italy (Ajello *et al.*, 1965; Caretta and Piontelli, 1975; Caretta *et al.*, 1992; Mancianti *et al.*, 1997), Pakistan (Mohammed *et al.*, 1971; Soomro *et al.*, 1990), Israel (Feuerman *et al.*, 1975), Kenya (Mohammed and Lalji, 1978), Spain (Calvo *et al.*, 1984; Guarro *et al.*, 1981; 1987 a, b; Gene *et al.* 1996; Cabanes *et al.*, 1997), France (Chabasse, 1988; Agut *et al.*, 1995), Jordan (Ali- Shtayeh, 1988; Ali- Shtayeh and Sheikh, 1988; Ali-Shtayeh and Arda, 1989), Zambia (Simpanya and Baxter, 1997) and Iran (Soleymani *et al.*, 2015).

In India, studies on mycokeratinophiles commenced with the work of Dey and Kakoti (1955), who isolated *Microsporum gypseum* from a soil sample collected from an animal house in Dibrugarh, Assam. Since then, a number of workers have reported occurrence of mycokeratinophiles from the soils of different states like Uttar Pradesh (Nigam and Kushwaha, 1985,1987; Mitra *et al.*, 1998), Rajasthan (Singh *et al.*, 1994), Maharashtra (Padhye and Thirumalachar, 1968), Orissa (Ghosh and Bhatt, 2000), Madhya Pradesh (Agnihotri and

Agarwal, 1989), Delhi (Randhawa and Sandhu, 1965), Chattisgarh (Deshmukh and Shukla, 2000), Tamil Nadu (Ramesh and Hilda, 1999), Jammu and Kashmir (Kaul and Sumbali, 1994, 2000a,b; Kotwal and Sumbali, 2011, 2014; Jandial and Sumbali, 2011; Deshmukh and Agarwal, 2003) and Andaman Islands (Dixit and Kushwaha, 1990).

Enrichment of soil with keratinous material is most conducive for the occurrence and growth of mycokeratinophiles (Padhye *et al.*, 1967; Otcenasek, 1978; Mercantini *et al.*, 1980, 1983). On the other hand, saline soils, dry- river sand, beach sand and barren road side soils have been reported as poor sources of mycokeratinophiles (Randhawa and Sandhu, 1965; Abdel- Fattah *et al.*, 1982). Report of some mycokeratinophiles like *Chrysosporium indicum* and *C. keratinophilum* in the soil of Antarctic region having a temperature of -4^{0}C are of considerable importance as it shows their adaptability and tolerance to freezing temperature (Caretta and Piontelli, 1977; Mercantini *et al.*, 1989; Del- Frate and Caretta, 1990). Similarly, occurrence and survival of mycokeratinophiles has also been reported from cold arid soils of Ladakh (Deshmukh *et al.*, 2010; Kotwal and Sumbali, 2011, 2014). Generally, mycokeratinophiles are considered to be mesophilic (Giuseppe *et al.*, 1987) but some strains are reported thermo-tolerant (Moharram *et al.*, 1988) and few reports indicate that they can adapt themselves to adverse temperatures for their survival (Pugh and Allsopp, 1982; Punsola and Guarro, 1984).

Mycokeratinophiles have also been categorized into various groups on the basis of vertical distribution in grassland and forest soils (Qureshi *et al.*, 2005). In both types of soil, the upper profiles contain the most diverse population. Moreover, the number of isolates from the deeper layers decreases as the distance from the upper surface increases. Chmel and Vlacilikova (1975) recovered mycokeratinophiles even from a depth of 55 cm. The differences in species number in soil profiles may be associated with adaptation to development at low partial pressure of oxygen and high carbon dioxide concentration in deep sites. The vertical distribution also seems to be associated with the concentration of keratinic substrates and with the composition of soil atmosphere. Rai and Qureshi (1994) found that mycokeratinophiles also differ in their substrate preference for colonization.

Mycokeratinophiles have also been reported from dung (Caretta *et al.*, 1976), sewage sludge (Ulfig and Koreez, 1983), school floor dust (Mercantini *et al.*, 1983), parks and gardens (Marsella *et al.*, 1985; Volz *et al.*, 1991; Caretta *et al.*, 1992; Vidyasagar *et al.*, 2005; Solari *et al.*, 2005; Mahmoudabadi and Zarrin, 2008; Sharma and Sharma, 2009), lake side soils (Govil *et al.*, 2001), hospital dust (Vidyasagar *et al.*, 2005), meteorite crater soils (Deshmukh and Verekar, 2006) and paddy soils (Shrivastava *et al.*, 2008) . In addition mycokeratinophiles have also been reported from feathers and nests of some birds (Ajello, 1953; Pugh, 1964, 65, 66; Otcenasek *et al.*, 1967; Rees, 1968; Hubalek, 1974).

Degradation of keratins by mycokeratinophiles

Mycokeratinophiles have the ability to cycle keratin, which is one of the most abundant and highly stable animal protein on the earth. Infact, these fungi possess the ability to degrade hard keratin and utilize it as a source of carbon, nitrogen and sulphur. Keratins (Greek word for 'horn'), which are insoluble fibrous proteins derived from the ectoderm are poorly biodegradable. According to Nelson and Cox (2005), there are two kinds of keratins (**Fig. 1**):

i) Alpha-keratins: These contain most of the common amino acids but are primarily rich in cystine residues and disulphide bridges. The rigid and brittle forms like horns and nails contain up to 22 per cent cystine, whereas the soft and flexible forms in the skin, hair and wool contain only 10 to 14 per cent. The alpha- keratins constitute an ecological problem as they are resistant to degradation by most of the microbes due to the tight packing of their polypeptide chains in the alpha-helix structures and due to their linkage by disulphide bridges (Marchisio, 2000).

ii) Beta-keratins: These lack both cystine and cysteine but are rich in amino acids with short side chains, especially glycine, alanine and serine. They are found in the fibers of spiders and silkworms, and in the scales, claws and beaks of reptiles and birds.

Due to the strength and stability of keratin, very few organisms are able to break it down and utilize it. These include few insects (e.g., the larvae of wool, feather and fur moths), helminths, bacteria (e.g., *Bacillus* species, thermophilic *Fervidobacterium pennavorans* and some actinomycetes), birds of prey, water moulds and some geophilic fungal species. Among these, the biggest group of organisms that can utilize keratin as the sole source of carbon, nitrogen and sulphur are the mycokeratinophiles belonging to *Ascomycetes*, *Zygomycetes* and *Chytridiomycetes* (Noval and Nickerson, 1959; Tribe and Abu-El-Souod, 1979).

Most of the ascomycetous keratinophiles belong to families *Arthrodermataceae* and *Onygenaceae* of the order *Onygenales* (Currah, 1985). The *Arthrodermataceae* and *Onygenaceae* are unusual in that majority of them are associated with birds and mammals. These are true mycokeratinophiles that vigorously degrade keratin and include important human and animal pathogens. Other commonly recovered mycokeratinophilic genera include *Chrysosporium*, *Geomyces*, *Malbranchea*, *Microsporum*, *Oideodendron*, *Sporendonema*, *Trichophyton* and their telomorphs (Kushwaha and Gupta, 2008).

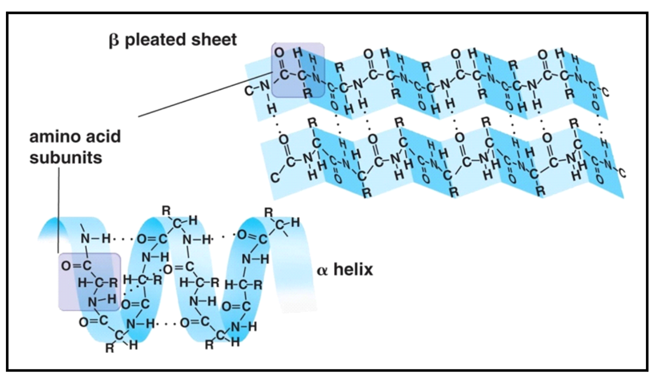


Fig. 1: Structure of alpha- and beta keratin (Nelson and Cox, 2005)

Ecological and biological significance

The ecological role of geophilic mycokeratinophiles is undoubtedly of prime importance as they degrade the keratinized material, which may be added to the soil from various sources in the form of feathers, hairs, nails, hoofs, horns, wool and related appendages as wastes. Hence, soil provides most conducive habitat for the growth and multiplication of keratinophilic fungi. In the soil, these fungi usually exist in their telomorphic (sexual) state, whereas on the keratinized material, they usually exist in an anamorphic (asexual) state in which they develop only a very simple morphology. When there is ample of keratin substrate available in the soil, these fungi multiply by asexual means by producing enormous number of conidia (aleuroconidia and arthroconidia). However, when the keratin substrate is depleted, these fungi reproduce by sexual means and form characteristic sexual fruiting bodies. The thick-walled sexual and some asexual spores are the propagules for the next generation and can remain dormant until fresh keratin or an alternative source of nutrition becomes available. In natural environments, keratinophilic fungi are involved in recycling of carbon, nitrogen and sulphur present in keratins by the action of three factors (Kunert, 2000):

- **i) Deamination.** Creating an alkaline environment needed for swelling, sulphitolysis and proteolytic attack.
- **ii) Sulphitolysis.** Denaturing the substrate by removing its disulphide bridges.
- **iii) Proteolysis.** Cleaving the denatured substrate to soluble products.

Mycokeratinophiles are vigorous and self- sufficient saprophytes as long as environmental conditions are favourable. However, they are opportunists and may become parasitic by accident. After becoming pathogenic, they are able to survive and multiply at host's body temperature, causing further infection by invading fresh keratinized tissues. Infection is transmitted from human to human or from animal to human by direct contact or by contact with infected hairs or epidermal cells. Infact, it is the only type of fungal infection known to be of contagious type. Such mycokeratinophiles, which cause diseases of skin and hair in man and animals, are commonly called as dermatophytes and their infections are known as cutaneous mycoses or dermatomycoses. These fungi, by virtue of their ability to colonize epidermal appendages, may become a source of sanitary danger to human health and accordingly, from time to time they have drawn the attention of various medical and veterinary epidemiologists. The dermatophytic fungi are keratinolytic in nature and belong to one of the three genera- *Microsporum*, *Trichophyton* or *Epidermophyton*. In addition to the dermatophytes, the non-dermatophytic mycokeratinophiles are emerging as leading cause of onychomycosis (Elewski, 1998; Raghavendra *et al.*, 2015).

The potential pathogenicity of mycokeratinophiles has been considered as a natural evolution from its presence in the soil (geophilic species) to invasion of cornified substrata in animals (zoophilic species) and man (anthropophilic species). Based on habitat, nature and epidemiology, dermatophytes are classified into three broad categories (Ajello, 1960):

i) Geophilic, which are saprobic, occur mainly in soil and are rarely pathogenic.

ii) Zoophilic, which are mainly parasitic to lower animals and are transmitted through contact.

iii) Anthropophilic, which are mainly parasitic to humans and cause dermatomycoses.

Molecular studies based on the DNA sequence analysis of the ribosomal ITS (Internal Transcribed Spacer) region have shown that these three groups are also phylogenetically distinct (Graser *et al*., 2000). The PCR based nucleic acid amplification procedures such as arbitrary primed PCR (AP-PCR) amplification techniques can rapidly distinguish dermatophytes and other keratinophilic fungal species examined through the generation of characteristic band patterns. Development of species-specific primers and probes for individual dermatophytes are more practical and precise methods for molecular detection (Pakshir *et al.,* 2013). In molecular identification, similarity and phylogeny of internal transcribed spacer (ITS) sequences of two related species is also studied (Woodgyer, 2004). These ITS regions of ribosomal DNA are used as primer and amplified. For isolation of a particular ITS region, specific restriction enzymes are used. Location of a specific gene in the genome is also used for molecular identification. Molecular markers also known as DNA markers which play important role for identification of particular species and are either PCR based or non PCR based methods. Molecular markers include Restriction Fragment length Polymorphism (RFLP), Random Amplified Polymorphic DNA (RAPD), Amplified Fragment length Polymorphism (AFLP), Simple Sequence Repeats (SSR), Inter Simple Sequence Repeats (ISSR), and Single Nucleotide Polymorphism (SNP), etc. Identification of dermatophytes by Matrix Assisted laser desorption ionization time-of-flight (MALDI-TOF) is reported by Erhard *et al.,* (2008). Molecular identification of mycokeratinophiles can also be done by purification of keratinase. Keratinase is separated by SDS-PAGE technique. The protein separation by SDS-PAGE is based on molecular weight of the compounds. In this technique polyacrylamide gel is used for separation. When electric field is applied, keratinase is separated according to molecular weight. For identification, the gel is stained with coomassie blue for 2 hours (El-Gayar *et al.*, 2012).

Mycokeratinophiles in causing Onychomycosis

Mycokeratinophiles cause infection of the nails also called as ungual mycosis or onychomycosis, a term derived from the Greek word “Onychos”, which means nail, and “mycosis” is an infection by fungi. The fungal invasion frequently causes hyperkeratosis reaction and a greater or lesser degree of destruction to the external layers or other structures of the nails (**Fig. 2**).

Onychomycosis generally means chronic fungal infection of toe nails and finger nails caused by different species of dermatophytes, saprophytic moulds, yeasts and yeast-like

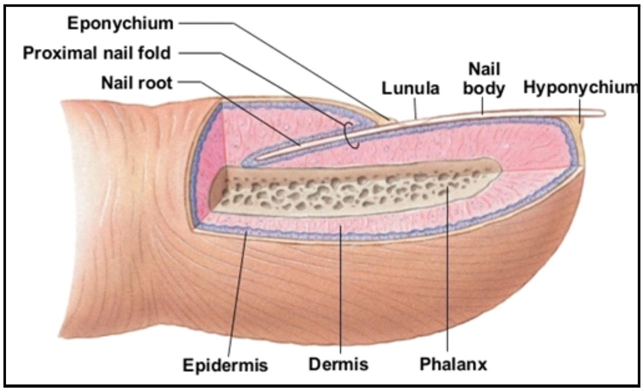


Fig. 2: Internal structure of the nail.

fungi. It is the most common nail disorder present in 2-13 per cent of general population, increasing up to 48 per cent by 70 years of age (Lilly *et al*., 2006). Onychomycosis caused by dermatophytes is called *Tinea unguium* (Anaissie *et al*., 2003) and the dermatophytic fungi causing it include species of *Trichophyton*, *Microsporum* and *Epidermophyton*. Other accountable non-dermatophytic species are yeast and yeast-like fungi, such as, species of *Candida*, *Geotrichum*, *Trichosporon* and saprophytic fungi like species of *Aspergillus*, *Alternaria*, *Cephalosporium*, *Scopulariopsis*, *Fusarium*, *Acremonium* and *Penicillium* (Khosravi and Mansouri, 2001). Mycokeratinophiles (both dermatophytes and non-dermatophytes) reported so far as causal agents of onychomycosis are listed in **table 1** and **table 2**.

Onychomycosis caused by dermatophytes is often symptomatic and can cause functional impairment. Its clinical appearance involves hyperkeratosis with thickening and discoloration of the nail plate. Other disorders such as nail psoriasis, lichen planus and nail trauma may yield a nearly identical picture (Scher and Baran, 2003).On the basis of their clinical appearance, onychomycosis is classified into four types (Roberts *et al*., 2003; Kaur *et al*., 2008):

i) Distal subungual onychomycosis (DSO): It is the most common form of *Tinea unguium*, in which the fungal infection invades the nail bed and the underside of the nail plate (**Fig. 3A**).

Table 1: Dermatophytic fungi associated with onychomycosis.

Dermatophytic fungi	Country	References
Trichophyton rubrum	Iceland Italy India Iran Pakistan	Gudnadottir *et al*., (1999) Romano *et al*., (2005) Kaur *et al*., (2008); Veer *et al*., (2007) Asadi *et al*., (2009) Farwa *et al*., (2011)
T. mentagrophytes	Iceland Italy India Iran Pakistan	Gudnadottir *et al*., (1999) Romano *et al*., (2005) Kaur *et al*., (2008); Veer *et al*., (2007) Asadi *et al*., (2009) Farwa *et al*., (2011)
T. violaceum	Italy Iran	Romano *et al*., (2005) Asadi *et al*., (2009)
T. tonsurans	Iran	Asadi *et al*., (2009)
T. verrucosum	Iran	Asadi *et al*., (2009)
T.simii	Spain	Torres-Rodriguez and Lopez-Jodra (2000)
T.concentricum	Spain	Torres-Rodriguez and Lopez-Jodra (2000)
T.megnini	Spain	Torres-Rodriguez and Lopez-Jodra (2000)
T. shoenleinii	Spain	Torres-Rodriguez and Lopez-Jodra (2000)
T. soudanense	Spain	Torres-Rodriguez and Lopez-Jodra (2000)
T. tonsurans	Spain Pakistan	Torres-Rodriguez and Lopez-Jodra (2000) Farwa *et al*., (2011)
T. interdigitale	Pakistan	Farwa *et al*., (2011)
Microsporum gypseum	India	Madhavi *et al*., (2011)
M. canis	Paris Tehran	Torres-Rodriguez and Lopez-Jodra (2000) Nowrozi *et al*., (2008)
M. audouinii	Tehran	Nowrozi *et al*., (2008)
Epidermophyton floccosum	Italy India Iran	Romano *et al*., (2005) Kaur *et al*., (2008) Asadi *et al*., (2009)

Table2: Non-dermatophytic fungi associated with onychomycosis.

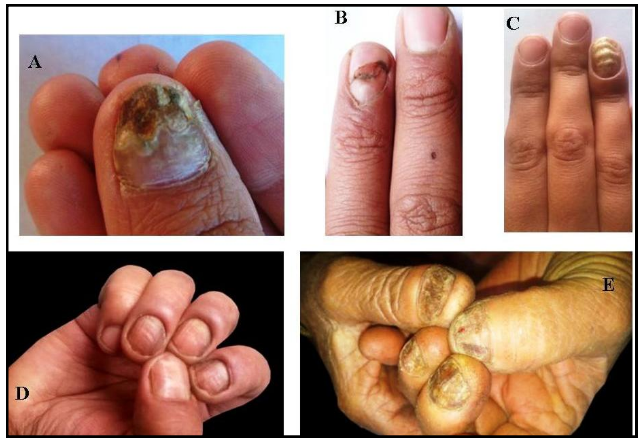
Non- Dermatophytic fungi	Country	References
Candida albicans	Italy, New York , India , Iran, Nigeria, Pakistan	Romano *et al*., (2005); Scher *et al*., (2007); Kaur *et al*., (2008), Veer *et al*., (2007); Asadi *et al*., (2009); Efuntoye *et al*., (2011); Farwa *et al*., (2011)
C. parapsilosis	Italy, Mexico, Korea, Chile	Romano *et al*., (2005); Manzano-Gayosso *et al*., (2008); Kim *et al*., (2013); Fich *et al*., (2014)
C. krusei	Italy, Pakistan	Romano *et al*., (2005); Farwa *et al*., (2011)
C. guilliermondii	Spain, Iran, Korea, Chile	Torres-Rodriguez and Lopez-Jodra (2000); Asadi *et al*., (2009); Kim *et al*., (2013); Fich *et al*., (2014)
C. tropicalis	Spain, Iran, Nigeria	Torres-Rodriguez and Lopez-Jodra (2000), Asadi *et al*., (2009), Efuntoye *et al*., (2011)
C. lipolytica	Mexico	Manzano-Gayosso *et al*., (2008)
C. glabrata	Mexico, Pakistan, Korea	Manzano-Gayosso *et al*., (2008); Farwa *et al*., (2011); Kim *et al*., (2013)
C. granuloma	Mexico	Manzano-Gayosso *et al*., (2008)
C. sake	Spain	Torres-Rodriguez and Lopez-Jodra (2000)
C. zeylanoides	Australia, Mexico	Crozier (1993); Manzano-Gayosso *et al*., (2008)
C. famata	Spain	Torres-Rodriguez and Lopez-Jodra (2000)
Aspergillus flavus	Spain, Iran, India	Torres-Rodriguez and Lopez-Jodra (2000); Asadi *et al*., (2009); Raghavendra *et al*., (2015)
A. sydowii	India, Spain	Wadhwani and Srivastava (1985); Torres-Rodriguez and Lopez-Jodra (2000)
A. fumigatus	Italy, Spain, Iran, Nigeria	Romano *et al*., (2005); Torres-Rodriguez and Lopez-Jodra (2000); Asadi *et al*., (2009); Efuntoye *et al*., (2011)
A. niger	India, Nigeria, India	Wadhwani and Srivastava (1985); Efuntoye *et al*., (2011); Raghavendra *et al*., (2015)
A. nidulans	Nigeria, India	Efuntoye *et al*., (2011); Shrihari *et al*., (2012)
A. glaucus	India	Shrihari *et al*., (2012)
A. tamarii	Denmark	Kristensen *et al*., (2005)
A. versicolor	Spain	Torres-Rodriguez and Lopez-Jodra (2000)
A. candidus	Spain	Torres-Rodriguez and Lopez-Jodra (2000)
A. terreus	Spain, Nigeria, India	Torres-Rodriguez and Lopez-Jodra (2000); Efuntoye *et al*., (2011); Shrihari *et al*., (2012)
A. persii	Italy	Zotti *et al*., (2010)
A. ustus	Spain	Torres-Rodriguez and Lopez-Jodra (2000)
A. nomius	Italy	Zotti *et al*., (2011)
Alternaria alternata	Pakistan USA	Farwa *et al*., (2011) Martinez-Herrera *et al*., (2015)
A. humicola	India	Wadhwani and Srivastava (1985)
A. pluriseptata	India	Wadhwani and Srivastava (1985)
Fusarium oxysporum	Canada, Brazil, Italy, India, Nigeria	Gupta *et al*., (2000); Godoy *et al*., (2004); Romano *et al*., (2005) ; Chithra *et al*., (2008); Efuntoye *et al*., (2011)
F. equiseti	India	Jandial and Sumbali (2012)
F. heterosporum	India	Jandial and Sumbali (2012)
F. solani	Canada, Brazil, Nigeria, Pakistan, India	Gupta *et al*., (2000); Godoy *et al*., (2004); Efuntoye *et al*., (2011); Farwa *et al*., (2011); Bhou and Sumbali (2015a)
F. proliferatum	India	Bhou and Sumbali (2015a)
F. moniliforme	Nigeria	Efuntoye *et al*., (2011)
F. dimerum	Pakistan, India	Farwa *et al*., (2011); Ranawaka *et al*., (2015); Ray *et al*.,(2016)
F. verticilloides	India	Bhou and Sumbali (2015a)
F. pallidoroseum	India	Bhou and Sumbali (2015a)
F. chlamydosporum	India	Bhou and Sumbali (2015a)
Penicillium marneffei	India	Ghosh *et al*.,(2015)
P. chrysogenum	Nigeria	Efuntoye *et al*., (2011)
P. notatum	Egypt	Batawi *et al*., (2006)
Cladosporium carrionii	India	Kaur *et al*., (2008)
C. sphaerospermum	India Pakistan	Kaur et al., (2008) Farwa *et al*., (2011)
C. cladosporioides	China	Shi *et al*., (2016)
Cryptococcus albidus	Mexico	Manzano-Gayosso *et al*.,(2008)
C. uniguttulates	Mexico	Manzano-Gayosso *et al*.,(2008)
C. laurentii	Mexico	Manzano-Gayosso *et al*.,(2008)
Chrysosporium keratinophilum	Mexico	Manzano-Gayosso *et al*.,(2008)
Cunninghamella bertholletiae	India	Tadepalli *et al*., (2015)
Chaetomium globusum	Japan, India, Canada, Korea, India	Hattori *et al*., (2000); Latha *et al*., (2010); Lagace and Cellier (2012); Kim *et al*., (2013); Bhou and Sumbali (2015b)

Table. 2 Contd.........

Non- Dermatophytic fungi	Country	References
Curvularia spp.	India	Veer *et al*., (2007); Pukhrambam *et al*., (2011)
Syncephalastrum racemosum	Serbia, Slovenia, India	Pavlovic and Bulaji (2006); Milos *et al*., (2006); Kumaran and Rudramurthy (2014); Baby *et al*., (2015)
Exophiala jeanselmei	France, India	Boisseau- Garsaud *et al*., (2002); Pukhrambam *et al*., (2011); Sharma *et al*.,(2012)
E. oligosperma	Taiwan	Wen *et al*., (2016)
Emericella quadrilineata	India	Gugnani *et al*., (2004)
Botryodiplodia theobromae	India	Kaur *et al*., (2008)
Onycochola canadensis	India	Kaur *et al*., (2008)
Scytalidium dimidiatum	New York, India, Iran, Pakistan	Scher *et al*., (2007); Kaur *et al*., (2008); Asadi *et al*., (2009); Farwa *et al*., (2011)
S. hyalinum	New York , India, Iran	Scher *et al*., (2007); Kaur *et al*., (2008); Asadi *et al*., (2009)
Geotrichum candidum	India	Kaur *et al*., (2008); Lungran et al., (2014)
Scopulariopsis brevicaulis	Belgium, Italy, India, Pakistan, Korea, Guatemala	Pierard (2001);Romano *et al*., (2005); Kaur *et al*., (2008); Farwa *et al*., (2011); Lee *et al*., (2012); Martinez –Herrera *et al*., (2015)
Acremonium potronii	Cleveland	Elewski (1998)
Trichoderma sp.	Turkey	Hilmioglu-Polat *et al*., (2005)
Cladophialophora carrionii	Pakistan	Farwa *et al*., (2011)
Ulocladium chartarum	Pakistan	Farwa *et al*., (2011)
U. botrytis	Italy	Romano *et al*., (2005)
Trichosporon asahii	Mexico	Manzano-Gayosso *et al*.,(2008)
T. mucoides	India, Italy	Sageerabanoo et al., (2011); Rizzitelli *et al*., (2016)
T. beigelii	India, Korea, Texas,	Vijaya *et al*., (2000); Kumar (2014); Han *et al*., (2000); Elmer *et al*., (2002)
Paecilomyces lilacinus	Italy	Innocenti *et al*., (2010)
P. variotii	Mexico	Arenas *et al*., (1998)
Rhizopus spp.	India, Malaysia, Guatemala	Pukhrambam *et al*., (2011); Shrihari *et al*., (2012); Leelavathi *et al*., (2012); Martinez –Herrera *et al*., (2015)
Mucor spp.	India	Pukhrambam *et al*., (2011); Shrihari *et al*., (2012)
Helminthosporium spp.	India	Kannan *et al*., (2006)
Hendersonula toruloidea	Nigeria	Gugnani *et al*., (1986)
Rhizomucor sp.	Malaysia	Leelavathi *et al*., (2012)
Nigrospora sphaerica	China	Fan *et al*., (2009); Huang *et al*., (2009)
Pichia ohmeri	Mexico	Manzano-Gayosso *et al*.,(2008)
Epicoccum spp.	India	Kumar (2014)
Absidia sp.	India	Shrihari *et al*., (2012)
Madurella spp.	Malaysia	Leelavathi *et al*., (2012)
Hortaea spp.	Malaysia	Leelavathi *et al*., (2012)
Aureobasidium sp.	Malaysia	Leelavathi *et al*., (2012)
Phialemonium spp.	Malaysia	Leelavathi *et al*., (2012)
Phialophora spp.	Malaysia	Leelavathi *et al*., (2012)
Pseudallescheria spp.	India Malaysia	Pukhrambam *et al*., (2011) Leelavathi *et al*., (2012)
Nattrassia spp.	Malaysia	Leelavathi *et al*., (2012)
Arthrographis spp.	Malaysia	Leelavathi *et al*., (2012)
Rhodotorula spp.	India Malaysia	Pukhrambam *et al*., (2011) Leelavathi *et al*., (2012)
Debaromyces spp.	Malaysia	Leelavathi *et al*., (2012)
Saccharomyces spp.	Malaysia	Leelavathi *et al*., (2012)
Sporobolomyces spp.	Malaysia	Leelavathi *et al*., (2012)
Scedosporium spp.	Finland	Issakainen *et al*., (2007)
Verticillium spp.	India	Pukhrambam *et al*., (2011)
Bipolaris spp.	India	Barua *et al*., (2012)
Auxarthron ostraviense	Czech Republic	Hubka *et al*., (2013)
A. umbrinum	Czech Republic	Hubka et al., (2013)
Gymnoascus dankaliensis	Guatemala	Chang *et al*., (2011)

ii) Proximal subungual onychomycosis (PSO): It refers to fungal penetration of the newly formed nail plate through the proximal nail fold. It is least common in healthy people, but more common when the patient is immuno-compromised (**Fig. 3B**).

iii) White superficial onychomycosis (WSO): It is caused by fungal invasion of the superficial layers of the nail plate forming "white islands" on the plate (Fig-3C).



Figs. 3(A-E): Different types of Onychomycosis- (A) Distal subungual onychomycosis (B) Proximal subungual onychomycosis (C) White superficial onychomycosis (D) Candidal onychomycosis and (E) Total dystrophic onychomycosis

iv) Candidal onychomycosis (CO): It refers to the invasion of finger nails by *Candida* species. It normally requires the prior damage of the nail by infection or trauma (**Fig. 3D**).

v) Total dystrophic onychomycosis (TDO): It refers to the total destruction of the nail plate, which usually may be the end result of any of the four main patterns of onychomycosis. The entire nail unit becomes thick and dystrophic. TDO is used to describe end-stage nail disease, although some clinicians consider it as a distinct subtype (**Fig. 3E**).

The most common symptom of a fungal nail infection is the thickening and discolouration of the nail, which takes up many colours like white, black, yellow or green. As the infection progresses, the nail may become brittle, with pieces breaking off or coming away from the toe or finger completely. If left untreated, the skin can become inflamed and painful underneath and around the nail. There may also be white or yellow patches on the nail bed or scaly skin next to the nail. The capacity of mycokeratinophiles to metabolise keratin of the nails is due to the production of extracellular keratinases, collagenases and elastases along with endopeptidases, lipases, glucosidases and nucleases (Torres-Rodriguez and Lopez-Jodra, 2000). These enzymes allow easy penetration and development of the mycelium, which further allows pathogenesis.

Until the late 1990s onychomycosis was a poorly discussed topic of medical science. Even in financially more advanced Asian countries, onychomycosis has been highlighted only in the last decade (Kaur *et al*., 2007). Onychomycosis affects approximately 5% of the population worldwide (Murray and Dawber, 2002) and represents 20-40% of onychopathies and about 30% of mycotic cutaneous infections (Achten and Wanet, 1978). In developing countries, higher priorities in socioeconomic concerns and health issues for other diseases, have resulted in low awareness of onychomycosis by physicians and the general public alike. In spite of improved personal hygiene and living environment, onychomycosis continues to spread and persist. The worldwide incidence of onychomycosis is increasing day by day and a number of factors contribute to this rise (Kaur *et al*., 2007). Firstly, as the population ages, there are corresponding chronic health problems that emerge, such as diabetes and poor peripheral circulation. Secondly, the number of persons who are immune-compromised because of infection with human immunodeficiency virus and the use of immunosuppressive therapies, cancer chemotherapy or antibiotics continue to expand. Thirdly, avid sports participation is increasing the use of health clubs, communal swimming pools and occlusive footwear for exercise. Additionally, in a small percentage of persons, onychomycosis may be caused by a genetic defect that causes alteration in immune function (Odom, 1994).

Though there is a clearly diseased appearance associated with this condition, onychomycosis is often regarded as merely a cosmetic problem of relatively minor importance that is hardly worth the effort to seek treatment in many cases. This belief may have been supported by the adverse effects and long dosing courses associated with some of the earlier antifungal agents (Kaur *et al*., 2008). However, in the last two decades there have been safe, effective systemic treatment regimes available for this chronic superficial fungal disease that can have significant negative effects on patients' emotional, social and occupational functioning. Although onychomycosis is rarely life threatening, its high incidence, prevalence and the associated morbidity, makes it an important public health problem.

REFERENCES

Abdel-Fattah, H.M., Moubasher, A.H. and Maghazy, S.M. 1982. Keratinolytic fungi in Egyptian soils. *Mycopath.* **79:** 49-53.

Achten, G. and Wanet, R.J. 1978. Onychomycosis in the laboratory. *Mykosen* **21:**125-127.

Agnihotri, S.K. and Agrawal, S.C. 1989. Keratinophilic fungi and related dermatophytes from the soils of Madhya Pradesh (India). *Proc. Nat. Acad. Sci. India* **59:** 193-196.

Agut, M., Bayo, M., Larrondo, J. and Calvo, M.A. 1995. Keratinophilic fungi from soil of Brittany, France. *Mycopath.* **129:** 81-82.

Ajello, L., Varsavsky, E., Sotgiu, G., Mazzoni, A. and Mamtovani, A. 1965. Survey of soils for human pathogenic fungi from the Emilia-Romagna region of Italy. *Mycopath. Mycol. Appl.* **26:** 65-70.

Ajello, L. 1953. The dermatophyte *Microsporum gypseum* as a saprophyte and parasite. *J. Invest. Derm.* **21:** 157-171.

Ajello, L. 1960. Geographic distribution and prevalence of dermatophytes. *Ann. New York Aca. Sci.* **89:** 30-38.

Ali-Shtayeh, M.S. 1988. Keratinophilic fungi isolated from children's sandpits in the Nablus area, West Bank of Jordan. *Mycopath.* **103:** 141-146.

Ali-Shtayeh, M.S. and Arda, H.M. 1989. Isolation of keratinophilic fungi from floor dust in Arab elementary and preparatory schools in the west bank of Jordan. *Mycopath.* **106:** 5-11.

Ali-Shtayeh, M.S. and Sheikh, B.S. 1988. Isolation of keratinophilic fungi from the floor dust of Arab kindergarten schools in the West Bank of Jordon. *Mycopath.* **103:** 69-73.

Anaissie, E.J., McGinnis, M.R. and Pfaller, M.A. 2003. *Clinical Mycology*. Philadelphia, Elsevier Sciences, 463-464.

Arenas, R., Arce, M., Munoz, H. and Ruiz-Esmenjaud, J. 1998. Onychomycosis due to *Paecilomyces variotii*. Case report and review. *J. Med. Mycol*. **8** (1):32-33.

Asadi, M.A., Dehghani, R. and Sharif, M.R. 2009. Epidemiologic study of onychomycosis and *Tenia pedis* in Kashan, Iran. *Jundishapur Journal of Microbiology* **2** (2): 61-64.

Baby, S., Ramya, T.G. and Geetha, R.K. 2015. Onychomycosis by *Syncephalastrum racemosum*: case report from Kerala, India. *Dermatology Reports* **7**:5527.

Barua, P., Borkotoki, U., Das, A., Barua, N., Barua, S., Mahanta, J., Barthakur, B.K. and Shivaprakash, M.R. 2012. Onychomycosis in green tea pluckers: a clinicomycological study. *Two and a Bud* **59** (2): 122-125.

Batawi, M.M.E., Arnaot, H., Shoeib, S., Bosseila, M., Fangary, M.E. and Helmy, A.S. 2006. Prevalence of non-dermatophyte molds in patients with abnormal nails. *Egyptian Dermatol. Online J.* **2** (1): 1-12.

Baxter, J. 1966. Isolation of *Trichophyton mentagrophytes* from British soil. *Sabouraudia.* **4**: 207-209.

Baxter, M. 1969. Keratinophilic fungi isolated from soil in the city of Birmingham, England. *Mycopath. Mycol. Appl.* **39**: 389-397.

Bertach, A. and Coello, N. 2005. A biotechnological process for treatment and recycling poultry feathers as a feed ingredient. *Bioresour. Technol.* **96** (15): 1703-1708.

Bhou, R. and Sumbali, G. 2015a. Fusarial onychomycosis-an unrecorded report from Jammu district (India). *Am. Int. J. Res. in Formal, Applied & Natural Sciences* **12** (1):21-26.

Bhou, R. and Sumbali, G. 2015b. Two cases of toenail Chaetomycosis from district Jammu (India). *Int. J. Pharmaceutical Sci. Invention* **4** (9): 9-12.

Boisseau-Garsaud, A.M., Desbois, N., Guillermin, M.L., Ossondo, M., Gueho, E. and Cales-Quist, D. 2002. Onychomycosis due to *Exophiala jeanselmei*. *Dermatology*. **204** (2):150-152.

Cabanes, F.J., Abarca, M.L. and Bragulat, M.R. 1997. Dermatophytes isolated from domestic animals in Barscelona, Spain. *Mycopath.* **137**: 107-113.

Calvo, A., Vidal, M. and Gurarro, J. 1984. Keratinophilic fungi from urban soils of Barcelona, Spain. *Mycopath.* **85**: 145-147.

Caretta, G. and Piontelli, E. 1975. Isolation of keratinophilic fungi from soil in Pavia, Italy. *Sabouraudia.* **13**: 33-37.

Caretta, G. and Piontelli, E. 1977. *Microsporum magellanicum* and *Cunninghamella antarctica*, new species isolated from Australia and Antarctic soil of Chile. *Sabouraudia.* **15**: 1-10.

Caretta, G., Frate, G.D., Piontelli, E. and Tadaro, F. 1976. Keratinophilic mycoflora of hair and dung of cows in fodder and in the soil on farms. Their distribution. *Riv. Parasite* **37**: 133-161.

Caretta, G., Mangiarotti, A.M. and Piontelli, E. 1992. Keratinophilic fungi isolated from soil of Italian parks in the province of Pavia. *Euro. J. Epidemiology* **8:** 330-339.

Carmichael, J.W. 1962. *Chrysosporium* and some other aleuriosporic Hyphomycetes. *Can. J. Bot.* **40:** 1137-1173.

Chabasse, D. 1988. Taxonomic study of keratinophilic fungi isolated from soil and some mammals in France. *Mycopath.* **101:** 133-140.

Chang, P., Moreno-Coutino, G. and Arenas, R. 2011. Mycotic Leukonychia in HIV Patients. Microbes, Viruses and Parasites in AIDS Process: In: *Tech. Janeza Trdine, Europe,* pp: 267-284.

Chithra, V., Rao, T., Sathiavathy, K., Suseela, K. and Binoy, K. 2008. Onychomycosis due to *Fusarium oxysporum*. *The Internet Journal of Infectious Diseases* **7** (2): 1-3.

Chmel, L. and Vlacilikova, A. 1975. The ecology of keratinophilic fungi at different depths of soil. *Sabouraudia.* **13:** 185-191.

Chmel, L., Hasilikova, A., Hrasco, J. and Vlacilikova, A. 1972. The influence of some ecological factors on keratinophilic fungi in the soil. *Sabouraudia.* **10:** 26-34.

Crozier, W.J. 1993. Two cases of onychomycosis due to *Candida zeylanoides*. *Australas J. Dermatol.* **34** (1):23-25.

Currah, R.S. 1985. Taxonomy of the *Onygenales*: *Arthrodermataceae, Gymnoascaceae, Myxotrichaceae* and *Onygenaceae*. *Mycotaxon.* **24:** 1-216.

Currah, R.S., Abbott, S.P. and Sigler, L. 1996. *Arthroderma silverra* sp. nov. and *Chrysosporium vallenarense*, keratinophilic fungi from arctic and mountain habitats. *Mycol. Res.* **100:** 195-198.

Daniels, G. 1954. Isolation of *Keratinomyces ajelloi* from soils in Great Britain. *Nature* **174:** 224-226.

Del-Frate, G. and Caretta, G. 1990. Fungi isolated from Antarctic material. *Polar Biology* **11**: 1-8.

Deshmukh, S.K. and Agrawal, S.C. 2003. Isolation of dermatophytes and other keratinophilic fungi from the soils of Jammu. *Mycoses* **46:** 226-228.

Deshmukh, S.K. and Shukla, R.V. 2000. Isolation of keratinophilic fungi from poultry farm soils of Chhattisgarh (India). *Kavaka* **28:** 55-58.

Deshmukh, S.K. and Verekar, S.A. 2006. Keratinophilic fungi from the vicinity of meteorite crater soils of Lonar (India). *Mycopath.* **162:** 303-306.

Deshmukh, S.K., Verekar, S.A. and Shrivastav, 2010. The occurrence of keratinophilic fungi in selected soils of Ladakh (India). *Natural Science* **2** (11): 1247-1252.

Dey, N.C. and Kakoti, L.M. 1955. *Microsporum gypseum* in India. *J. Ind. Med. Assoc.* **25**: 160-164

Dixit, A.K. and Kushwaha, R.K.S. 1990. Keratinophilic fungi of Andaman Islands, India. *Ind. J. Microbiol.* **30:** 349-350.

Duries, E.B. and Frey, D. 1955. Isolation of *Microsporum gypseum* and *Keratinomyces ajelloi* from Australian soil. *Nature* **176:** 936.

Efuntoye, M.O., Sobowale, A.A., Mabekoje, O.O. and Agu, G.C. 2011. Onychomycosis among rural farmers in a southwestern part of Nigeria. *Egyptian Dermatol. Online J.* **7** (1):1-9.

Elewski, B.E. 1998. Onychomycosis: Pathogenesis, Diagnosis and Management. *Clinical Microbiol. Reviews* **11** (3): 415-429.

El-Gayar, K.E., Zaghloul, T.I., Haroun, M.A. and Saeed, H.M. 2012. Purification of Alkaline Protease from Hydrolyzed Chicken Feather Waste Using Recombinant *B. Subtilis* Strain. *Scientific J. King Faisal University (Basic and Applied Sciences)* **13** (1): 139-151.

Elmer, K.B., Elston, D.M. and Libow, L.F. 2002. *Trichosporon beigelii* infection presenting as white piedra and onychomycosis in the same patient. *Cutis*. **70** (4): 209-211.

Emmons, C.W. 1942. Isolation of *Coccidioides* from soil and rodents. *US Public Health Repts.* **57:** 109-111.

Erhard, M., Hipler, U.C., Burmester, A., Brakhage, A.A. and Wostemeyer, J. 2008. Identification of dermatophyte species causing onychomycosis and *Tinea pedis* by MALDI-TOF mass spectrometry. *Exp. Dermatol.* **17** (4):356-361.

Fan, Y.M., Huang, W.M., Li, W. and Zhang, G.X. 2009. Onychomycosis caused by *Nigrospora sphaerica* in an immunocompetent man. *Arch. Dermatol.* **145** (5): 611-612.

Farwa, U., Abbasi, S.A., Mirza, I.A., Amjad, A., Ikram, A., Malik, N. and Hanif, F. 2011. Non- dermatophyte moulds as pathogens of onychomycosis. *J. College of Physicians and Surgeons Pakistan* **21** (10): 597-600.

Feuerman, E., Alteras, I., Honig, E. and Lehrer, N. 1975. The isolation of keratinophilic fungi from soil in Israel. *Mycopath.* **56:** 41-46.

Fich, F., Abarzua-Araya, A., Perez, M., Nauhm, Y. and Leon, E. 2014. *Candida parapsilosis* and *Candida guillermondii*: Emerging Pathogens in Nail Candidiasis. *Indian J. Dermatol.* **59** (1): 24-29.

Gene, J., Guillamol, J.M., Ulfig, K. and Guarro, J. 1996. Studies on keratinophilic fungi. X. *arthrographis alba* sp. nov. *Can. J. Microbiol.* **42**: 1185-1189.

Ghosh, S.D., Chakraborty, M., Mitra, A. and Bhattacharyya, I. 2015. Case Study: *Penicillium marneffei* causing onychomycosis: 2 rare case reports. *Int. J. Curr. Res.* **7** (6): 17040-17042.

Ghosh, G.R. and Bhatt, S. 2000. Keratinophilic fungi from Chilka lake-side soil Orissa (India). *Ind. J. Microbiol.* **40:** 247-254.

Giuseppe, C., Giuseppe, D.F., Paola, D.F., Maria, G., Maria, M.A. and Elena, S. 1987. Mesophilic, thermophilic and keratinophilic fungi in a rice field soil and phylloplane fungi. *Boletin. Micologico.* **3** (2): 117-121.

Godoy, P., Nunes, F., Silva, V., Tomimori-Yamashita, J., Zaror, L. and Fischman, O. 2004. Onychomycosis caused by *Fusarium solani* and *Fusarium oxysporum* in Sao Paulo, Brazil. *Mycopath.* **157**: 287-290.

Govil, N., Bhatnagar, V.P., Kumar, A., Mathur, M. and Srivastava, J.N. 2001. Biodiversity of keratinophiles in Indian hills (Shimla, H.P.) and plains (Agra, U.P.). *J. Ind. Bot. Soc.* **80:** 183-186.

Graser, Y., Hoog, G.S. de. and Kuijpers, A.F.A. 2000. Recent advances in the molecular taxonomy of dermatophytes. In: *Biology of dermatophytes and other keratinophilic fungi* (Eds.: Kushwaha, R.K.S. and Guarro, J.). Revista Iberoamericana de Micologia, Spain; pp. 17-21.

Guarro, J., Punsola, L. and Calvo, M.A. 1981. Keratinophilic fungi from soil of Terragona, Catalunya. *Mycopath.* **76:** 69-71.

Guarro, J., Punsola, L. and Cano, J. 1987a. *Byssoonygena ceratinophila*, gen. et sp. nov. a new keratinophilic fungus from Spain. *Mycopath.* **100:** 159-161.

Guarro, J., Punsola, L. and Figueras, M.J. 1987b. *Brunneospora reticulata*, gen. et sp. nov. a keratinophilic Ascomycete from Spain. *Persoonia* **13**: 387-390.

Gudnadottir, G., Hilmarsdottir, I. and Sigurgeirsson, B. 1999. Onychomycosis in Icelandic Swimmers. *Acta. Dermato. Venereologica* **79:** 376-377.

Gugnani, H.C., Nzelibe, F.K. and Osunkwo, I.C. 1986. Onychomycosis due to *Hendersonula toruloidea* in Nigeria. *J. Med. Vet. Mycol.* **24** (3): 239-41.

Gugnani, H.C., Vijayan, V.K., Tyagi, P., Sharma, S., Stchigel, A.M. and Guarro, J. 2004. Onychomycosis due to *Emericella quadrilineata*. *J. Clin. Microbiol.* **42** (2): 914-916.

Gupta, A.K., Jain, H.C., Lynde, C.W., MacDonald, P., Cooper, E.A. and Summerbell, R.C. 2000. Prevalence and epidemiology of onychomycosis in patients visiting physicians' offices: A multicenter Canadian survey of 15,000 patients. *J. Am. Acad. Dermatol.* **43** (2): 244-248.

Han, M.H., Choi, J.H., Sung, K.J., Moon, K.C. and Koh, J.K. 2000. Onychomycosis and *Trichosporon beigelii* in Korea. *Int. J. Dermatol.* **39** (4):266-269.

Hattori, N., Adachi, M., Kaneko, T., Shimozuma, M., Ichinohe, M. and Iozumi, K. 2000. Case report: Onychomycosis due to *Chaetomium globosum* successfully treated with itraconazole. *Mycoses* **43** (1-2): 89-92.

Hilmioglu-Polat, S., Metin, D.Y., Inci, R., Dereli, T., Kilinc, I. and Tumbay, E. 2005. Non-dermatophytic molds as agents of onychomycosis in Izmir, Turkey a prospective study. *Mycopath.* **160:** 125-128.

Huang, W.M., Fan, Y.M., Li, W. and Zhang, G.X. 2009. Superficial white onychomycosis caused by *Nigrospora sphaerica*: a case report. *Chinese J. Dermatol.* **42** (8): 522-524.

Hubalek, Z. 1974. Fungi associated with free living birds in Czechoslovakia and Yugoslovokia. *Acta Sci. Nat. Acad. Sci. Bohem. Bmo.* **8:** 1-71.

Hubka, V., Dobiasova, S., Lyskova, P., Mallatova, N., Chlebkova, J., Skorepova, M., Kubatova, A., Dobias, R., Chudickova, M. and Kolarik, M. 2013. *Auxarthron ostraviense* sp. nov., and *A. umbrinum* associated with non-dermatophytic onychomycosis**.** *Med. Mycol.* **51:** 614-624.

Innocenti, P., Pagani, E., Vigl, D., Pasquetto, V., Scalzo, K. and Larcher, C. 2010. Onychomycosis by *Paecilomyces lilacinus* in a patient with leukonychia. *Microbiologia Medica* **25** (1): 52-53.

Jandial, S. and Sumbali, G. 2012. Fusarial onychomycosis among gardeners: A report of two cases. *Indian J. Dermatol. Venereol. Leprol.* **78:**229.

Jandial, S. and Sumbali, G. 2011. Diversity of Keratinophilic fungi from the botanical garden soil of North Indian University of Jammu**.** *Proc. Nat. Acad. Sci. India.* **81:** 359-365.

Kannan, P., Janaki, C. and Selvi, G.S. 2006. Prevalence of dermatophytes and other fungal agents isolated from clinical samples. *Indian J. Med. Microbiol.* **24** (3): 212-215.

Kaul, S. and Sumbali, G. 1994. Prevalence of soil borne keratin degrading fungi in dairy farm soils of Jammu (J&K). *Geobios* **21:** 54-59.

Kaul, S. and Sumbali, G. 2000a. Keratinophilic fungi from poultry farm soil of Jammu, India. *Mycologist.* **14:** 289-291.

Kaul, S. and Sumbali, G. 2000b. Keratinophilic fungi from feathers of Indian poultry birds. *Mycologist.* **14:** 13-15.

Kaur, R., Kashyap, B. and Bhalla, P. 2007. A five-year survey of onychomycosis in New Delhi, India: Epidemiological and Laboratory aspects. *Indian J. Dermatol.* **52** (1): 39-42.

Kaur, R., Kashyap, B. and Bhalla, P. 2008. Onychomycosis-Epidemiology, diagnosis and management. *Indian J. Medical Microbiol.* **26** (2): 108-116.

Khosravi, A.R. and Mansouri, P. 2001. Onychomycosis in Tehran, Iran: prevailing fungi and treatment with itraconazole. *Mycopath.* **50**: 9-13.

Kim, D.M., Lee, M.H., Suh, M.K., Ha, G.Y., Kim, H. and Choi, J.S. 2013. Onychomycosis caused by *Chaetomium globosum. Ann. Dermatol.* **25** (2): 232-236.

Kominami, M. 1961. A survey of keratinolytic or keratinophilic moulds from soil in Japan. Report III. The identification of *Trichophyton lipoferum* sp. nov. *Jap. J. Med. Mycol.* **2:** 38-41.

Kotwal, S. and Sumbali, G. 2011. Incidence of myco-keratinophiles in cold arid soil at high altitude Khardung village of Ladakh, India. *J. Mycol Pl. Pathol.* **41:** 72-76.

Kotwal, S. and Sumbali, G. 2014. Comparative analysis of keratinophilic fungi from the soils of Khardung and Khardung La (Ladakh), India. *Biolife J.* **2** (4): 1326-1331.

Kristensen, L., Stenderup, J. and Otkjaer, A. 2005. Onychomycosis due to *Aspergillus tamarii* in a 3-year-old boy. *Acta Derm. Venereol.* **85** (3):261-62.

Kumar, S. 2014. Clinico-Mycological study of onychomycosis in HIV positive patients. *Online Int. Interdisciplinary Res. J.* **4:** 142-147.

Kumaran, R. and Rudramurthy, K.G. 2014. Total dystrophic onychomycosis caused by *Syncephalastrum recemosum*: A Case Report. *Int. J. Scientific Study.* **2** (9): 115-116.

Kunert, J. 2000. Physiology of keratinophilic fungi. In: Biology of dermatophytes and other keratinophilic fungi. (Eds.: Kushwaha, R.K.S. and Guarro, J.) *Revista Iberoamericana de Micologia*, Spain; pp. 66-76.

Kushwaha, R.K.S. and Gupta, P. 2008. Relevance of keratinophilic fungi. *Curr. Sci.* **94**: 706-707.

Lagace, J. and Cellier, E. 2012. A case report of a mixed *Chaetomium globosum/ Trichophyton mentagrophytes* onychomycosis. *Medical Mycology Case Reports* **1**: 76-78.

Latha, R., Sasikala, R., Muruganandam, N. and Prakash, M.R.S. 2010. Onychomycosis due to ascomycete *Chaetomium globosum*: A case report. *Indian J. Pathol Microbiol.* **53** (3): 566-567.

Lee, M.H., Hwang, S.M., Suh, M.K., Ha, G.Y., Kim, H. and Park, J.Y. 2012. Onychomycosis caused by *Scopulariopsis brevicaulis*: Report of two cases. *Ann. Dermatol.* **24** (2): 209-213.

Leelavathi, M., Tzar, M.N. and Adawiah, J. 2012. Common microorganisms causing onychomycosis in tropical climate. *Sains Malaysiana* **41** (6): 697-700.

Lilly, K.K., Koshnick, R.L., Grill, J.P., Khalil, Z.M., Nelson, D.B. and Warshaw, E.M. 2006. Cost-effectiveness of diagnostic tests for toenail onychomycosis: A repeated measure, single-blinded, cross-sectional evaluation of seven diagnostic tests. *Am Acad Dermatol.* **55**: 620-626.

Lungran, P., Pukhrambam, P.D., Mate, H. and Golmei, A. 2014. Prevalence and etiological agents of onychomycosis. *Indian Medical Gazette* **147** (7): 397-402.

Madhavi, S., Rama Rao, M.V. and Jyothsna, K. 2011. Mycological study of dermatophytosis in rural population. *Annals of Biological Res.* **2** (3): 88-93.

Mahmoudabadi, A.Z. and Zarrin, M. 2008. Isolation of dermatophytes and related keratinophilic fungi from the two public parks in Ahvaz, Jundishapur. *J. Microbiol.* **1**: 20-23.

Mancianti, F., Mignone, W. and Papini, R. 1997. Keratinophilic fungi from coats of wild boars in Italy. *J. Wildlife Diseases* **33:** 340-342.

Manzano-Gayosso, P., Hernandez-Hernandez, F., Mendez-Tovar, L.J., Palacios-Morales, Y., Cordova-Martinez, E., Bazan-Mora, E. and Lopez-Martinez, R. 2008. Onychomycosis Incidence in Type 2 Diabetes Mellitus Patients. *Mycopath.* **166:** 41-45.

Marchisio, V.F. 2000. Keratinophilic fungi: Their role in nature and degradation of keratinic substrates. In: Biology of dermatophytes and other keratinophilic fungi. (Eds.: Kushwaha, R.K.S. and Guarro, J.) *Revista Iberoamericana de Micologia, Spain;* pp. 86-92.

Marples, M.J. 1965. The distribution of keratinophilic fungi in soils from New Zealand and from two Polynesian Islands. *Mycopath. Mycol. Appl.* **25:** 361-372.

Marsella, R., Mercantini, R., Spinelli, P. and Volterra, L. 1985. Occurrence of keratinophilic fungi in animals of the Zoological park of Rome. *Mykosen.* **28:** 507-512.

Martinez-Herrera, E.O., Arroyo-Camarena, S., Tejada-Garcia, D.J., Porras-Lopez, C.F. and Arenas, R. 2015. Onychomycosis due to opportunistic molds. *An Bras. Dermatol.* **90** (3):334-337.

Mercantini, R., Marsella, R. and Cervellati, M.C. 1989. Keratinophilic fungi isolated from Antarctic soil. *Mycopath.* **106:** 47-52.

Mercantini, R., Marsella, R., Caprilli, F. and Dovgiallo, G. 1980. Isolation of dermatophytes and correlated species from the soil of public gardens and parks in Rome. *Sabouraudia.* **18:** 123-128**.**

Mercantini, R., Marsella, R., Labiase, L. and Fulvi, F. 1983. Isolation of keratinophilic fungi from floors in Roman primary schools. *Mycopath.* **82:** 115-120.

Milos, D., Pavlovic, M.D. and Bulajic, N. 2006. Great toenail onychomycosis caused by *Syncephalastrum racemosum. Dermatol. Online J.* **12:** 7.

Mitra, S.K., Sikdar, A. and Das, P. 1998. Dermatophytes isolated from selected ruminants in India. *Mycopath.* **142:** 13-16.

Mohammed, M., Khan, K.A. and Anwar, A.A. 1971. Isolation and study of keratinophilic fungi from West Pakistan soil. *J. Sci. (Karachi).* **1**: 144-158.

Mohammed, S.I. and Lalji, N. 1978. The distribution of geophilic dermatophytes in Kenyan soils. *Mycopath.* **63:** 95-97.

Moharram, A.M., Abdel-Gawad, K.M. and Mohamed el-Maraghy, S.S. 1988. Ecological and physiological studies on fungi associated with human hair. *Folia Microbiol.* (Praha) **33** (5): 363-371.

Murray, S.C. and Dawber, R.P. 2002. Onychomycosis of toenails: orthopaedic and podiatric considerations. *Australas J. Dermatol.* **43:**105-112.

Nelson, D.L. and Cox, M.M. 2005. *Lehninger Principles of Biochemistry.* WH Freeman and Co., New York; Pp. 1-1119.

Nigam, N. and Kushwaha, R.K.S. 1985. Eight new keratinophilic fungal records from India. *Proc. Nat. Acad. Sci. India.* 55th Ann. Sess. 26.

Nigam, N. and Kushwaha, R.K.S. 1987. Seven new keratinophilic fungal records from India. *Kavaka* **15:** 29-31.

Noval, J.J. and Nickerson, W.J. 1959. Decomposition of native keratin by *Streptomyces fradiae*. *J. Bact.* **77:** 251-263.

Nowrozi, H., Nazeri, G., Adimi, P., Bashashati, M. and Emami, M. 2008. Comparison of the activities of four antifungal agents in an *in-vitro* model of dermatophyte nail infection. *Indian J Dermatol.* **53** (3): 125-128.

Odom, R.B. 1994. Common superficial fungal infections in immunosuppressed patients. *J. Am. Acad. Dermatol.* **31** (3):56-59.

Otcenasek, M. 1978. Ecology of the dermatophytes. *Mycopath.* **65:** 67-72.

Otcenasek, M., Hedec, K., Hubalek, Z. and Dvork, J. 1967. Keratinophilic fungi from the nests of birds in Czechoslovakia. *Sabouraudia.* **5:** 350-354.

Otsenasek, M. and Dvorak, J. 1964. The isolation of *Chrysosporium keratinophilum* (Frey) Carmichael (1962) and similar fungi from Czechoslovakia soil. *Mycopath. Mycol. Appl.* **23:** 121-122.

Padhye, A.A. and Thirumalachar, M.J. 1968. Distribution of *Allescheria boydii* Shear in soil of Maharashtra state. *Hindus. Antibio. Bull.* **10:** 200-201.

Padhye, A.A., Pawar, V.H., Sukapure, R.S. and Thirumalachar, M.J. 1967. Keratinophilic fungi from marine soils of Bombay, India Part I. *Hindus. Antibio. Bull.* **10:** 138-141.

Padhye, A.A., Shekhon, A.S. and Carmichael, J.W. 1973. Ascocarp production by *Nannizia* and *Arthroderma* on keratinous and non-keratinous media. *Sabouraudia.* **11**: 109-114.

Pakshir, K., Ghiasi, M.R., Zomorodian, K. and Gharavi, A.R. 2013. Isolation and molecular identification of keratinophilic fungi from public parks soil in Shiraz, Iran. *BioMed. Research Int.* **2013**:1-5.

Pavlovic, M.D. and Bulajic, N. 2006. Great toenail onychomycosis caused by *Syncephalastrum racemosum. Dermatol. Online J.* **12 (**1):7.

Pierard, G. 2001. Onychomycosis and other superficial fungal infections of the foot in elderly: A Pan-European survey. *Dermatology* **202**: 220-224.

Pugh, G.J.F. 1964. Dispersal of *Arthroderma curreyi* by birds and its role in the soil. *Sabouraudia* **3:** 275-278.

Pugh, G.J.F. 1965. Cellulolytic and keratinophilic fungi *recorded on birds. Sabouraudia* **4:** 85-95.

Pugh, G.J.F. 1966. Association between bird's nests, their pH and keratinophilic fungi. *Sabouraudia* **4:** 49-53.

Pugh, G.J.F. and Allsopp, D. 1982. Microfungi on Signy Island, South Orkney Islands. *Brit. Antarct. Surv. Bull.* **57:** 55-67.

Pukhrambam, P.D., Devi, K.R. and Singh, N.B. 2011. Pattern of Onychomycosis- A RIMS Study. *J. Commun. Dis.* **43** (2): 105-112.

Punsola, L. and Guarro, J. 1984. *Keratinomyces ceretanicus* sp. nov., a psychrophilic dermatophyte from soil. *Mycopath.* **85:** 185-190.

Qureshi, S., Agrawal, S.C. and Rai, M.K. 2005. Keratinophilic fungi: Diversity and sensitivity to some medicinal herbs. In: *Fungi: Diversity and Biotechnology.* (Ed. Rai, M.K. and Deshmukh, S.K.) Scientific Publishers, Jodhpur, India; pp. 455-480.

Raghavendra, K.R., Yadav, D., Kumar, A., Sharma, M., Bhuria, J. and Chand, A.E. 2015. The nondermatophyte molds: Emerging as leading cause of onychomycosis in South-East Rajasthan. *Indian Dermatol. Online J.* **6** (2): 92-97.

Rai, M.K. and Qureshi, S. 1994. Screening of different keratin baits for isolation of keratinophilic fungi. *Mycoses*. **37:** 295-298.

Ramesh, V.M. and Hilda, A. 1999. Incidence of keratinophilic fungi in the soil of primary school and public parks of Madras city, India. *Mycopath.* **143:** 139-145.

Ranawaka, R.R., Nagahawatte, A., Gunasekara, T.A. 2015. *Fusarium* onychomycosis: prevalence, clinical presentations, response to itraconazole and terbinafine pulse therapy, and 1-year follow-up in nine cases. *Int. J. Dermatol.* **54** (11):1275-1282.

Randhawa, H.S. and Sandhu, R.S. 1965. A survey of soil inhabiting dermatophytes and related keratinophilic fungi of India. *Sabouraudia*. **4:** 71-79.

Ray, R., Ghosh, M., Chatterjee, M., Chatterjee, N. and Banerjee, M. 2016. Case Report: Onychomycosis caused by *Fusarium dimerum. J. Clin. Sci. Res*. **5**: 44-48.

Rees, R.G. 1968. Keratinophilic fungi from Queensland II and III. Isolation from feathers of wild birds. *Sabouraudia*. **6**: 14-28.

Repova, A. 1990. Soil micromycetes from Czechoslovakia. A list of isolated species with bibliography. IV. *Ceska. Mykologie* **44:**170-176.

Rippon, J.W. and Medenica, M. 1964. Isolation of *Trichophyton soudanense* in the United States. *Sabouraudia*. **3:** 301-302.

Rizzitelli, G., Guanziroli, E., Moschin, A., Sangalli, R. and Veraldi, S. 2016. Case report: Onychomycosis caused by *Trichosporon mucoides. Int. J. Infectious Diseases* **42**: 6163

Roberts, D.T., Taylor, W.D. and Boyle, J. 2003. Guidelines for treatment of onychomycosis. *Br. J. Dermatol.* **148**: 402-410.

Romano, C., Papini, M., Ghilardi, A. and Gianni, C. 2005. Onychomycosis in children: a survey of 46 cases. *Mycoses*. **48:** 430-437.

Sageerabanoo, Malini, A., Oudeacoumar, P. and Udayashankar, C. 2011. Onychomycosis due to *Trichosporon mucoides*. *Indian J. Dermatol. Venereol. Leprol.* **77** (1):7677.

Scher, R.K. and Baran, R. 2003. Onychomycosis in clinical practice: factors contributing to recurrence. *Br. J. Dermatol.* **149**: 5-9.

Scher, R.K., Tavakkol, A., Sigurgeirsson, B., Hay, R.J., Joseph, W.S., Tosti, A., Fleckman, P., Ghannoum, M., Armstrong, D.G., Markinson, B.C. and Elewski, B.E. 2007. Onychomycosis: Diagnosis and definition of cure. *J. Am. Acad. Dermatol.* **56** (6): 937-944.

Sharma, A., Chauhan, S., Gupta, P. and Guleria, R.C. 2012. A Case of Onychomycosis which was caused by *Exophiala Jeanselmei. J. Clinical and Diagnostic Res.* **6** (6): 1081-1082.

Sharma, M. and Sharma, M. 2009. Influence of environmental factors on the growth and sporulation of geophilic keratinophiles from soil samples of public park. *Asian J. Exp. Sci.* **21**: 307-312.

Shi, D., Lu, G., Mei, H., Shen, Y., Qiu, Y. and Liu, W. 2016. A rare case of onychomycosis induced by *Cladosporium cladosporioides*. *Open J. Clinical and Medical Case Reports* **2** (2): 1-6.

Shih, J.C.H. 1993. Recent development in poultry waste digestion and feather utilization: A review. *Poult. Sci.* **72:** 1617-1620.

Shih, J.C.H. and Wang, J.J. 2006. Keratinase technology: from feather degradation and feed additive, to prion destruction.CAB Rev.: *Perspt. Agric., Vet. Sci., Nutr. Nat. Resour.* **42:** 1-6.

Shrihari, N., Kumudini, T.S., Mariraj, J. and Krishna, S. 2012. The prevalence of keratomycosis, dermatophytosis, and onychomycosis in a tertiary care hospital. *Int.J. Medical and Health Sciences* **1** (3): 25-30.

Shrivastava, J.N., Satsangi, G.P. and Kumar, A. 2008. Incidence of keratinophilic fungi in water logged condition of paddy soil. *J. Environmental Biology* **29:** 125-126.

Simpanya, M.F. and Baxter, M. 1997. Isolation of fungi from soil using the keratin- baiting technique. Zambia. *Mycopath.* **136:** 85-89.

Singh, C.J., Singh, B.G. and Singh, B.S. 1994. Keratinophilic fungi of Ghana bird's sanctuary, Bharatpur (Rajasthan). *Adv. Plant Sci.* **7:** 280-294.

Solari, N., Guglielminetti, M. and Caretta, G. 2005. Seasonal behaviour of keratinophilic fungi isolated from park's soil in Milan. *Boletin. Micologia* **20:** 9-13.

Soleymani, A., Sefidgar, S.A.A., Hoseini, M. and Sharifi, H. 2015. Species Diversity of Keratinophilic Fungi in Various Soil Type of Babol Medical University's Hospitals' Yard, Iran. *Int. J. App. Sci. and Tech.* **5** (3): 55-59.

Soomro, I.H., Zardari, M., Mangi, S. and Abro, H. 1990. Isolation and identification of dermatophytes and other keratinophilic fungi from the soil of Shah Abdul Latif University, Khairpur, Sindh, Pakistan. *Scientific Khyber.* **3:** 175-182.

Srivastava, O.P., Jain, M. and Shukla, P.K. 1990. A critical review on keratinophilic fungi. (Ed.: Hasija, S.K. and Bilgrami, H.S.) In: *Perspectives in Mycological Research II.* Prof. GP Agarwal Festschrift: 269-292. Today and Tomorrow's Printers and Publ. New Delhi.

Szathmary, S. 1936. Origin of Dermatophyton. *Hung. Med. Arch.* 37: 394-398.

Tadepalli, K., Gupta, P.K., Asati, D.P. and Biswas, D. 2015. Onychomycosis due to *Cunninghamella bertholletiae* in an Immunocompetent Male from Central India. *Case Reports in Infectious Diseases* **2015**:1-4.

Taylor, W.W., Radcliffe, F. and Paenen, V. 1964. The isolation of pathogenic fungi from the soils of Egypt, The Sudan and Ethiopia. *Sabouraudia*. **2:** 235-236.

Torres-Rodriguez, J.M. and Lopez-Jodra, O. 2000. Epidemology of nail infection due to Keratinophilic fungi. In: *Biology of dermatophytes and other keratinophilic fungi*. (Eds.: Kushwaha, R.K.S. and Guarro, J.). Revista Iberoamericana de Micologia, Spain; pp. 122-135.

Tribe, H.T. and Abu-El-Souod, S.M. 1979. Colonization of hair in soil-water cultures, with especial reference to the genera *Pilimelia* and *Spirillospora* (*Actinomycetales*). *Nova Hedwigia* **31:** 789-805.

Ulfig, K. and Koreez, M. 1983. Isolation of keratinophilic fungi from sewage sludge. *Sabouraudia* **21:** 247-250.

Vanbreuseghem, R. 1952. Keratin digestion by dermatophytes; a specific diagnostic method. *Mycologia* **44:** 176-182.

Veer, P., Patwardhan, N.S. and Damle, A.S. 2007. Study of onychomycosis: Prevailing fungi and pattern of infection. *Ind. J. Medical Microbiol.* **25** (1): 53-56.

Vidyasagar, G.M., Narayan, H. and Shivkumar, D. 2005. Keratinophilic fungi isolated from hospital dust and soils of public places at Gulbarga, India. *Mycopath.* **159:** 13-21.

Vijaya, D., Anand, B.H.K., Nagarathamma, T. and Joseph, M. 2000. Case reports: Onychomycosis caused by *Trichosporon beigelii. Indian J. Dermatol. Venereol. Leprol.* **66** (2): 93-94.

Vollekova, A. 1984. *Microsporum persicolor* and other keratinophilic fungi in soil and in a rodent's den. *Biologia Czechoslovakia* **39:** 899-904.

Volz, P.A., Wlosinki, M.J. and Warser, S.P. 1991. Sparse diversity of potential pathogenic soil micro-fungi in the Ukraine (USSR). *Microbios.* **65:** 187-194.

Wadhwani, K. and Srivastava, A.K. 1985. Some cases of onychomycosis from North India in different working environments. *Mycopath.* **92:** 149-155.

Wang, J.J., Borwornpinyo, R. and Shih, J.C.H. 2007. Sup35 NM- His 6 aggregates: a prion-like protein useful in prion degradation studies. *Enz. Microb. Tech.* **36:** 758-765.

Wen, Y.M., Rajendran, R.K., Lin, Y.F., Kirschner, R. and Hu, S. 2016. Onychomycosis associated with *Exophiala oligosperma* in Taiwan. *Mycopath.* **181:**83-88.

Woodgyer, A. 2004. The curious adventures of *Trichophyton equinum* in the realm of molecular biology: a modern fairy tale. *Med. Mycol.* **42** (5):397-403.

Youssef, Y.A., El-din, A.A.K. and Hassanein, S.M. 1992. Occurrence of keratinophilic fungi and related dermatophytes in soils in Cairo, Egypt. *Zentral blatt Fuer Mikrobiologie.* **147:** 80-85.

Zotti, M., Machetti, M., Perotti, M., Barabino, G. and Persi, A. 2010. A new species, *Aspergillus persii*, as an agent of onychomycosis. *Med. Mycol.* **48**: 656-660.

Zotti, M., Machetti, M., Persi, A., Barabino, G., Parodi, A. 2011. Onychomycosis: first case due to *Aspergillus nomius*. *Acta Derm. Venereol.* **91** (5):591-592.