INTRODUCTION

Dermatophytes are the fungi that invade the keratinized and cutaneous areas of the body (nail, hair and skin). Most of them belong to the ***hyphomycetes*** but several are now known to have perfect states (teleomorphs) in the family ***Gymnoascaceae*** of the order ***Eurotiales*** **(Rippon, 1974 and Emmons *et al.*, 1977).**

The dermatophytes are represented by three major genera of pathogenic molds: ***Microsporum***, ***Trichophyton***, and ***Epidermophyton*** on the basis of morphology of their macro and microconidia. The teleomorphs of the ***Microsporum*** and ***Trichophyton*** spp. are called nannizia and arthroderma respectively, however asexual form of *Epidermophyton floccosum* is unknown **(Barbara *et al.*, 1994).**

Dermatophytoses (cutaneous mycoses) produce enzymes that enable them to degrade keratinized tissue. These enzymes include keratinase, elastase and collagenase, which break down keratin, elastin and collagen respectively. All of these substrates are components of epithelial and connective tissues **(Robert, 1995).**

Many fungi that cause diseases have developed mechanisms that ease their survival and reproduction within the hostile environment. In this way, dermatophytes elaborate the enzyme keratinase, which hydrolyzes the structural protein of keratin. But the dermatophytes (cutaneous mycoses) are also limited to keratinized tissues of the epidermis, hair, and nails **(Cutler, 1991; Lincoff and Mitchel, 1977; Maresca and Kobayashi, 1996 and Perfect, 1996).** The inability of dermatophytes to invade deep tissue is probably related to the fact that they grow optimaly at 25°C, which the temperature of the outer dead layers of skin is lower than body temperature. In addition, dermatophytes are unable to convert to alternative growth forms, as do the dimorphic

fungi. Other factors such as oxidation – reduction potential and tissue conditions are probably also involved as barriers to dermatophytes infection (**Patrick *et al.*, 1998 and Robert, 1995).**

Humidity is the more important environmental factor for penetration of dermatophytes into the stratum corneum than temperature. At least 90% humidity is necessary for penetration of dermatophytes into stratum corneum within a few days. Mean humidity in the interdigital space between the 4th and 5th toes was found to be approximately 98% **(Junya *et al.*, 1998).** Many dermatophyte characteristically perforate hairs in vitro by means of special hyphal appendages called perforating organs. Under controlled conditions, perforation of hair appears to be reliable way of differentiating ***Trichophyton mentagrophytes*** from ***Trichophyton rubrum*** **(Rebell and Taplin, 1970).**

Dermatophytes Infections (Tinea cases or dermatomycosis)

In fact, fungi have a major influence on the health and people throughout the world. They cause a wide spectrum of clinical diseases, from simple cosmetic problems to potentially lethal systemic infections (Moselio *et al.*, 1998).

Dermatophytes abound world wide as saprophytes in the soil but many of them have evolved to a parasitic existence. Dermatophytes are strict parasites of humans. Some of them are no longer found in the soil, while others can be found in the lower order animals. Finally, some are found free in nature and accidentally cause infection in humans. The cutaneous mycoses are the only contagious fungal disease in humans **(Robert, 1995).**

Dermatophyte infections are also referred to as ringworm or tinea. The term tinea comes from Latin and means "worm" or "moth". It describes the serpentine (snake like) and annular (ring like) lesions on

the skin that resemble worm burrowing at the margin. The modifying terms that indicate the anatomical sites involved: ***Tinea pedis***, feet; *Tinea capitis*, scalp; ***Tinea manus***, hands; ***Tinea ungium***, nails; and *Tinea corporis*, body (**Patrick *et al.*, 1998 and Stanley *et al.*, 1994).**

Antifungl Agents (Drugs)

Selective action against fungi without toxic side effect is difficult to achieve because fungal cells like mammalian cells are eukaryotic. However there is a number of useful antifungal agents that are highly specific for fungal cells and nontoxic to the parasitized host cells **(Elliott *et al.*, 1997, Chandler *et al.*, 1980 and Kwon-Chung and Bennett, 1992)**. Toxicity is a problem in the treatment of fungal disease, in addition many antifungal compounds have limited therapeutic value because of problems with solubility, stability and absorption. Compared to antibacterial agents, the number of effective antifungal agents are quite small. This result indicates an increase in frequency of fungal infection (**Medoff *et al.*, 1983 and Sutcliffe and Georgopapadakou, 1992).**

The antifungal agents used in treating systemic fungal infections fall into three major classes of compounds: polyenes, azoles, and nucleoside derivatives.

i-Polyenes are secondary metabolites produced by various species of *Streptomyces*. They are cyclic macrolide lactones containing variable number of hydroxyls, and form two to seven conjugated double bonds. These compounds are classified by their amount of ring structure unsaturation (e.g., diene, triene, tetraene, pentaene, hexaene and heptaene). Although the action mechanism of these compounds is complex, it is based primarily on the ability of these compounds to bind to sterols in the cytosolic membranes of susceptible cells, because fungal

membranes contain ergosterol, mammals contain cholesterol, plants contain sitosterol. This fact is the basis for the toxicity of these compounds when they are used to treat patients with systemic fungal infections. The only clinically useful polyene is amphotericin B because its great potency for fungal cells damage than mammalian cells (**Anker *et al.*, 1995; Perfect, 1996 and Yamaguchi *et al.*, 1992**).

ii-Azole derivatives The azole derivatives constitute the largest group of antifungals that are commercially available. They have a broad spectrum of activity against fungi and to some extent Gram-positive bacteria. These compounds are fungistatic and act by blocking biosynthesis of ergosterol resulting in leakage of cell contents. They may cause transit abnormalities of liver function. Severe hepatotoxicity is a rare complication of ketoconazole therapy (**Anker *et al.*, 1995 and Elliott *et al.*, 1997**).

iii-Nucleoside analogues 5-fluorocytosine is a polar fluorinated pyrimidine that has a narrow spectrum of activity against certain fungi. It is deaminated in fungal cell to 5-fluorouracil that is incorporated into RNA in place of uracil resulting in abnormal protein of DNA synthesis. Resistance may arise during treatment. It is well absorbed from the gastrointestinal tract with low protein binding, metabolically stable, and exhibits high bioavailability in humans. Unfortunately, it has a narrow spectrum of antifungal activity and rapidly induces resistance in susceptible organisms. (**Anker *et al.*, 1995; Georgopapadakou and Walsh, 1996 and Yamaguchi *et al.*, 1992**).

Production of antifungal (antidermatophytes) by actinomycetes

Actinomycetes have gained great economic and public health importance as producers of antibiotics antifungal, vitamins and enzymes. The majority of antibiotics producing actinomycetes are found in *Sterptomyces* species. This led to a growing economic importance of these organisms, with approximately 93% producing secondary metabolites (**Ellaiah *et al.*, 1998**).

Heptaene antibiotics are fungicidal macrolides produced by *Streptomyces* species (**Martin and Mc-Daniel, 1977**). The best known compound of this class, amphotericin B, and some other structurally related antibiotics have been applied in therapy because of their powerful and broad spectra of activity. Despite having been in use for almost 40 years and in spite of its limited tolerability, amphotricin B has lost none of its importance. This antibiotic is often the drug of first choice in increasing number of life threading fungal infections (**Georgopapadakou and Walsh, 1996**). Numerous heptaene containing compounds has proved too toxic for therapeutic use, and so interest in new heptaene macrolides has wand sharply in the last 25 years.

Micromonospora is another important genus having the ability to produce several antibiotics as hazimicins, spartnomicins A&B and other antibacterial (**Wagman and Weinstein, 1980; Marquez *et al.*, 1983 and Nair *et al.*, 1992**).

Effect of essential oils on dermatophytes.

Essential oils derived from many plants are known to possess biological activity against prokaryotic (**Deans and Ritchie, 1987; Janssen *et al., 1987***) and eukaryotic organisms (**Thompson, 1989**).

Aromatic and medicinal plants have proved to be an important resource of biologically active compounds useful in medicine and plant protection **(Jacobson, 1958; Jurd and Manners, 1980; Trease and Evans, 1985 and Towers *et al.*, 1989).**

Recently many studies on the antifungal activities of the essential oils have been reported **(Garg and Siddiqui, 1992; Daouk *etal.*, 1995; Shimoni *et al.*, 1993; Muller-Riedau *et al.*, 1995 and Thompson, 1989).** Most of these are focused on the antifungal activities of essential oils against soil borne pathogens **(Shimoni *et al.*, 1993 and Muller-Riebau *et al.*, 1995)** and food storage fungi **(Mishra and Dubey, 1994 and Kishore *et al.*, 1993).**

Essential oils extracted from some plants have proved their potential for use as natural fumigants in controlling the fungal deterioration of some foods during storage **(Dwivedi and Dubey, 1993).** However, there is only limited information in the literature on the antifungal activity of essential oils toward human fungal pathogen.

Activity of propolis against dermatophytes

Propolis (bee glue), a natural product derived from plant resins collected by the honeybees, has been used for thousands of years in folk medicine for several purposes. The extract of propolis containing amino acids, phenolic compounds, phenolic esters, flavonoids, cinnamic acid, terpenes and caffeic acid, possess several biological activities such as anti-inflammatory, immunostimulatory, antifungal and antibacterial **(Cardile *et al.*, 2003).**