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## INTRODUCTION

Fungal infections have become a very serious problem to humans, animals and plants. Further, *Fusarium* spp. includes a number of soil borne species that distributed worldwide have been known for a long time as important plant pathogens (Roncero *et al.*, 2003). *Fusarium* spp. are responsible for a variety of plant diseases such as Fusarium wilt in tomatoes, ear rot in corn, head blight and scab in barley and wheat. *Fusarium oxysporum* f. sp. *asparagi* and *Fusarium proliferatum* are the most severe pathogens of asparagus causing fusarium crown and root rot (Hang and Woodams, 2003). The most common species, *F. oxysporum*, causes vascular wilt disease in a wide variety of economically important crops (Roncero *et al.*, 2003).

The pathogenic *Fusarium* spp. also produced a number of toxins (fumonisin, zearalenone, deoxynivalenol, T – 2 toxins) that can cause human illness such as alimentary toxic aleukia and massive intoxication of horses, swine, calves and poultry (Hang and Woodams., 2003). More recently, *Fusarium* has also been reported as an emerging human pathogen in patients. *F. oxysporum* is an anamorphic species characterized by a series of morphological criteria including the shape of macroconidia, structure of microconidiophores and formation and disposition of chlamydo spores (Roncero *et al.*, 2003).

*Candida* infections are a major cause of morbidity and mortality in compromised hosts. *Candida albicans*, *C. tropicalis* and *C. parapsilosis* are most frequently involved in systemic infections. The majority of these infections are endogenous in origin and gastrointestinal colonization, mucosal invasion and blood stream spread are the stages of the most common route of endogenous *Candida* infections (Mellado *et al.*, 2000).

*Candida* spp. are the fourth most commonly recovered organism from all blood cultures of hospitalized individuals, with an estimated crude mortality rate of 38 to 75%. Nosocomial candidiasis, recognized as an important cause of morbidity and mortality, has been mainly described in neutropenic patients as well as in intensive care and post-surgery units. The majority of candidemia was due to *C. albicans*, but many reports have documented an increasing incidence of *C. tropicalis*, *C. glabrata*, *C. krusei*, *C.*

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*parapsilosis*, and *C. kefyr* as nosocomial pathogens. These species cause fungal infections particularly in neonatal intensive care and in neutropenic patients (Mohammed *et al.*, 2005).

*Saccharomyces* spp. has been reported to cause thrush, vulvovaginitis and fungemia. The most common species of the genus in the clinical laboratory is *S. cerevisiae* and *S. pombe* (Warren and Hazen, 1999).

Nowadays, the need for new, safe and more effective antifungal agent is a major challenge to the pharmaceutical industry today, especially with the increase in opportunistic infections in the immuno compromised host. Among the different types of drug prevailing in the market, antifungal antibiotics are a very small but significant group of drugs and have an important role in the control of mycotic diseases (Gupte *et al.*, 2002).

Nevertheless, very few effective antifungal agents are available. One reason for the slow progress compared to antibacterial is that, like mammalian cells, fungi are eukaryotes; and therefore agents that inhibit protein, RNA or DNA biosynthesis in fungi have greater potential for toxicity to the host as well. The second reason is that, until recently, the incidence of life-threatening fungal infections was perceived as being too low to warrant aggressive research by the pharmaceutical companies (Gupte *et al.*, 2002).

The history of new drug discovery processes show that novel skeletons have, in the majority of cases, come from natural sources. This involved the screening of microorganisms and plant extracts, using a variety of models (Gupte *et al.*, 2002). The medicines from natural sources should not be overlooked because they have the properties that are very important in the medical field such as:

- a. they cause no harm and place no additional stress on the body
- b. they help the body to adapt to various environmental and biological stresses
- c. they have non - specific action on the body, supporting some or all of the major systems, including nervous, hormonal and immune systems, as well as regulatory functions (Ng, 2004).

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Thus, some fungi may have beneficial effects while others are pathogenic. One group of fungi, the mushrooms, are abundant in proteins. In fact mushrooms form favourite dishes in the Oriental as well as the Western cuisines. A variety of proteins with interesting biological actions were produced by fungi and many of these proteins have potential application (Ng, 2004).

An example, macrofungi are mainly represented by mushrooms. They are widely distributed in nature, many are edible and some are highly medicinal. Attempts have been made in many parts of the world to explore the use of mushrooms and their metabolites for the treatment of a variety of human ailments. A recent survey indicated that a large number of antifungal agents were produced by fungi (Ajith and Janardhanan, 2003). Alveolarin, a novel antifungal polypeptide from wild mushroom, *Polyporus alveolaris* is active against a number of fungal species, like *Botrytis cinera*, *F. oxysporum*, *Mycosphaerella arachidicola* and *Physalospora piricola* (Wang *et al.*, 2004).

Another example, a 15 kDa antifungal protein, designated as ganodermin, was isolated from the medicinal mushroom *Ganoderma lucidum*. Ganodermin inhibits the mycelial growth of *B. cinerea*, *F. oxysporum* and *P. piricola*. It is devoid hemagglutinating, deoxyribonucleases, ribonucleases and protease inhibitory activities. It is indeed; fair to describe all major medicinal mushroom preparations, both cellular compounds and secondary metabolites, having weak antigenicity and with no side effects (Solomon, 2002).

The safety of mushroom based dietary supplements was further enhanced through the following controls:

- a. the overwhelming majority of mushrooms used for production of medicinal application were cultivated commercially (and not gathered in the wild). This guaranteed proper identification and pure, unadulterated products. In many cases it also means genetic uniformity. This may also benefit conservation of biodiversity.
- b. many mushrooms were easily propagated vegetative and thus keep as one clone. The mycelium could be stored for a long time, the genetic and biochemical consistency may be checked after a considerable period of time.

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- c. many edible and medicinal mushrooms were capable of growing in the form of mycelial biomass in submerged cultures (Solomon, 2002).

There are about 14000 species of mushrooms in the world. They may contain a vast and yet largely untapped source of powerful new pharmaceutical products. Biologically active substances isolated from mushrooms as fruit bodies, cultured mycelium and culture broth exhibit promising activity against *in vivo* and *in vitro* (Mao *et al.*, 2005).

In lignin modifying enzymes production, basidiomycetes causing white-rot are the most efficient lignin degraders in nature. Biomass is available in large quantities in the forest. This has to be degraded to return elements to the environment. Degradation is brought about by sets of extracellular oxidoreductases (peroxidases, laccases) (Nuske *et al.*, 2002). The ligninolytic system of fungi that cause white-rot has been extensively studied in recent years, especially with respect to their enzymatic potential for the bioremediation of persistent pollutants (Rothschild *et al.*, 2002).

Malaysia, well known for its tropical forests, is an ideal place for the growth of many plants, due to its wide range of light intensities, water quantities and nutrient levels. This causes inter-specific competition and the climate created by the abundant vegetation is also very suitable for insects, fungi and other organisms (Kool *et al.*, 2005). The vast fungal diversity is yet to be exploited for pharmaceuticals and non-pharmaceutical applications. The polypores are least exploited except for *Ganoderma* spp. (Chang *et al.*, 1993) and *Trametes* spp. (Ng, 1998). In Malaysia, there is a growing interest in the polypores as sources of bioactive agents.

The aims of this study are to investigate indigenous polypores as the sources of antifungal agents as well as possible lignin modifying enzymes producers. The specific objectives were:

- a. to screen selected polypores for antifungal activity.
- b. to select culture system for the production of antifungal agents.
- c. to screen selected polypores for lignin modifying enzymes activity.