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Ghulam Murtaza
PMAS-Arid Agriculture University, Rawalpindi, Pakistan

Muhammad Mukhtar
Department of Biotechnology, American University of Ras Al Khaimah, UAE

Aysha Sarfraz
Quaid-i-Azam University, Islamabad, Pakistan, aysharizvi87@gmail.com

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A REVIEW: ANTIFUNGAL POTENTIALS OF MEDICINAL PLANTS

Ghulam Murtaza[1], Muhammad Mukhtar[2], Aysha Sarfraz[3]*

[1] PMAS-Arid Agriculture University, Rawalpindi 46300, Pakistan.

[2]. Department of Biotechnology, American University of Ras Al Khaimah PO Box 10021, Ras Al Khaimah, UAE.

[3] Quaid-i-Azam University , Islamabad 44400, Pakistan.

*Email: aysharizvi87@gmail.com

ABSTRACT

Medicinal plants have been widely used to treat a variety of infectious and non-infectious diseases. According to an estimate, 25% of the commonly used medicines contain compounds isolated from plants. Several plants could offer a rich reserve for drug discovery of infectious diseases, particularly in an era when the latest separation techniques are available on one hand, and the human population is challenged by a number of emerging infectious diseases on the other hand. Among several other ailments, fungal infections are posing a great threat to the mankind, as a large number of people suffer from fungal infections worldwide due to emerging resistance of fungal strains. The available antifungal drugs are either too costly or are accompanied with several side effects. Of importance, a variety of medicinal plants have shown promise to treat a number of fungal infections, and some of them possess broad-spectrum antifungal activity. This article describes potential antifungal properties of medicinal plants against fungi, and suggests screening the potential of plants possessing broad-spectrum antifungal effects against emerging fungal infections.

Keywords: Medicinal Plants, Conventional medicine, fungal infection, antifungal.

INTRODUCTION

Fungal infections are the leading cause of death in both advanced and developing countries. This is due to the use of immunosuppressive treatments, long term use of antibiotics, and longer survival of immunocompromised individuals (Molero et al., 1998**)**.

There are numerous antifungal agents used clinically to treat fungal infections. Triazole antifungal agents like fluconazole and itraconazole came into play in the early 1990’s, followed by amphotericin-B in the mid 1990’s. These antifungal drugs can be broadly classified into five major classes, i.e. azoles, allylamines, echinocandins, griseofulvin, and flucytosine (Chen and Sorrell, 2007).

The emerging resistance of microbes to antifungal agents has serious implications in the management of infections. These antifungal compounds also act on targets found in mammalian cells which may result in toxicity or adverse drug interactions (Lucca and Walsh, 1999). Ketoconazole is one of the antifungal drugs used against both superficial and deep seated infections.

However, its unpleasant side effects include nausea, abdominal pain, itching, toxicity, slow therapeutic response, and poor efficacy in immunocompromised patients (Pyun and Shin, 2005).

Therefore, the discovery of novel antifungals is severely needed. Phytochemistry of various plant species has indicated that the phytochemicals could be a better source of medicine as compared to synthetically produced drugs. The use of plants as medicine goes back to early man. These traditional medicines based on medicinal plants have been used for centuries. Therefore one approach that has been used for discovery of antimicrobial agents is the evaluation of plant extracts (Ozcelic et al., 2005).

Medicinal plants are of great importance to health of individuals and communities. This importance lies in their chemical substances that produce a definite physiological action on the human body. The most important of these bioactive compounds include alkaloids, tannins, flavonoids, and phenolic compounds (Edeoga et al., 2005). The health effects of flavonoids include antioxidant, anti-inflammatory, antiallergic, hepatoprotective, antithrombotic, antiviral, and anti-carcinogenic (Prior, 2003). Alkaloids show many useful effects like anti-hypertensive and anti-tumor. Alkaloid based drugs include caffeine, quinine, nicotine, artemisinin**,** cholchicine, and amblyopia (Taber et al., 2002). Tannins include corilagin and geraniin, which show anti-human immuno deficiency syndrome activity by inhibiting reverse transcriptase (Notka et al., 2004).

Emerging Fungal Pathogens

Fungal pathogens are a leading cause of morbidity and mortality in immunocompromised patients. Several of these pathogens are well known, e.g. *Aspergillus fumigatus. Aspergillus fumigatus* is the major cause of nosocomial fungal pneumonia and is the cause of the second most common fungal infections. The antifungal drug Azole was effective against this pathogen but now it has started developing a resistance against it (Moye-rowley, 2015). Fungal keratitis, an infection of the cornea, is caused by a rare *Trichophyton spp*. (Sharma et al., 2014). *Cryptococcus neoformans* is the cause of CNS mycosis in HIV-infected patients (Price et al., 2011). *Histoplasma capsulatum* causes a rare infection, Histoplasmosis, which typically targets mammals. It has a latent stage can be reactivated when the patient is immunocompromised (Rappleye et al., 2004). There is also recognition of other emerging fungal infections, such as *Fusarium* spp, Zygomycetes and dematiaceous moulds, dimorphic fungi such as *Penicillium marneffei*, *Coccidioides inmotis*, and *Histoplasma capsulatum* (Walsh and Groll, 1999).

Candida spp. has been found to be fourth leading cause of nosocomial infections (Pfaller and Diekema, 2007). They caused about 88% of infections in the United States between 1980 and 1990. *Candida albicans* is the species most commonly isolated from clinical material and accounts for 40-70 % of cases of candidiasis. The epidemiology data indicates that 5 to 10 of every 1000 risk patients will contract *Candida* blood stream infection and about 35 % of these patients will die as a result of infection, while 30 % will die as a result of an underlying disease (Lockhart et al., 2009). In 2013, it was reported by the Centers for Disease Control (CDC) in the United States that a resistant strain of *Candida albicans* is responsible for approximately 3,400 cases of both superficial and blood stream infections, annually.

In addition to humans, plants are also greatly affected by different fungal infections. *Puccinia spp.* causes different types of rust diseases in wheat and is a reason for great losses in grain production (McIntosh et al., 1995). *Fusarium graminearum* causes a disease called Fusarium head blight in wheat and barley (Ding et al., 2009). *Alternaria* species is among the most common cause of necrotrophic diseases of plants. Some of the major plant pathogens reside in this genus, including *A. brassicicola* and *A. solani*. *A. brassicicola* is the cause of black spot disease on an important plant species of *Brassica* (Westman et al., 1999). *Synchytrium endobioticum,* a soil-borne obligate biotrophic fungus, is the cause of potato wart disease in the cultivated potato (*Solanum tuberosum L*.) (Obidiegwu et al., 2014)

Ustilago maydis is a member of the biotrophic smut fungi that infects grasses and many important crop plants such as maize, wheat, barley, and sugar cane (Brefort et al., 2009).

Medicinal Values of Plants

The recent research on medicinal plants has revealed their great pharmacological importance due to the presence of active phytoconstituents. Medicinal substances are products of metabolic pathways. Nevertheless, each species has its own genetic structure that governs the presence of bioactive molecules. Environmental effects are also responsible for variations in the amount of phytochemicals present in each species (Thomas, 2000).

About 80% of the world depends on alternative medicines from plants. Approximately 70, 000 plants are used in medicines. Indian Ayurveda utilizes about 2,000 plants to cure different ailments. These plants are our common heritage and their use for human use has developed the concept of herbal medicine or phytotherapy. Every medicinal herb contains a number of constituents that facilitate its curative activity. A few of these compounds include reserpine, taxol, and vincristine, which have been isolated and synthesized on a large scale. The total number of compounds present in the plant kingdom is about 200, 000. These compounds are used by plants for maintenance, reproduction, healing, defense, and offense. The plants are used for their nutrients in general, and to some extent for the healing process. Many of these food plants possess polyphenols and antioxidants. Vegetable, fruits and nuts are also a good source of secondary metabolites (Daniel, 2006). A summary of medicinal plants having antifungal effects have been given in table 1.

Isolation and Characterization of Antifungal Compounds

The very basic and essential step for the evaluation of therapeutic potential of medicinal plants is preparation of a crude extract, followed by isolation of various medicinal constituents. There are a large number of books and literature available regarding phytomedicines. Some examples are *Plant Drug Analysis: A Thin Layer Chromatography Atlas* (Wagner et al., 1996), *Modern Phytomedicine: Turning Medicinal Plants into Drugs* (Ahmad et al., 2007) and *Laboratory Handbook for the Fractionation of Natural Extracts* (Houghton and

Table 1: Medicinal Plants used against different pathogenic fungi.

	Medicinal Plants	Antifungal activity	References
1.	*Eucalyptus globolus, Punica granatum, Artemisia mexcana* and *Bocconia arborea*	The methanolic plant extracts possess strong *in vitro* anticandidal activity	Navarro *et al.* 1996
2.	*Micromeria nervosa* and *Inula viscose*	Ethanolic and aq. extracts were tested and show antifungal activity	Ali-Shtayeh et al. 1998
3.	*Hypericum scabum, Thymus fallax*	Trichloromethanolic, n-hexane, aqueous aerial parts, bulb and seed of plants show anticandidal activity.	Atalay et al. 1999
4.	*Rhoicissus digitata* and *Rhoicissus rhomboidea*	Methanolic extract of root exhibited highest anticandidal activity.	Lin et al. 1999
5.	*Albiizia lebbeck, Allium sativum, Allium cepa, Cassia angustifolia, Coriandrum sativum, Moringa pterygosperma, Tamarindus indica, Tectona grandis and Zingiber officinale*	Aqueous extracts of plants used to cure Candidiasis.	Srinivasan et al. 2001
6.	*Rubus ulmifolius*	Methanolic extract of leaves, branches and flowering tops showed a larger inhibition zone against *Candida albicans.*	Panizzi et al. 2002
7.	*Terminalia chebula*	Methanolic and aqueous extract of seed of plant show anticandidal activity	Vonshak *et al*. 2003
8.	*Syzygium jambolanum*	Leaf, fruit, stem, bark showed anticandidal activity.	Chandraekaran *et al*. 2004
9.	*Zanthoxylum americanum*	Aqueous extracts show antifungal activity	Bafi-Yeboa *et al*. 2005
10.	*Justicia secunda and Piper pulchrum*	Methanolic extract of plant show anticandidal activity	Rojas *et al*. 2006
11.	*Schinus terebintifolis, Ocimum gratissimum, Cajanus cajan and Piper aduncum*	Methanolic extracts of different parts show anticandidal activity.	Braga *et al.* 2007
12.	*Piper ovatum Vahl*	C. tropicalis	Silva *et al*., 2009
13.	*Mentha piperita*	Antifungal activities against *Candida* and *Aspergillus spp.*	Saharkhiz *et al*., 2012
14.	*Achillea millefolium*	Anticandidal activity	Ribeiro *et al*., 2010
15.	*Cymbopogon citratus*	Antifungal activity against *Malassezia spp.*	Carmo *et al*., 2013
16.	*Boesenbergia pandurata*	Antifungal activity against *Candida albicans*	Taweechaisupapong *et al*., 2010
17.	*Xanthium strumarium L.*	Essential oil inhibits growth of *Candida albicans* and *Aspergillus niger*	Rad *et al*., 2015
18.	*Oxalis corniculata*	crude, *n*-hexane, and chloroform extracts show activity against *Fusarium solani*, *Aspergillus flexneri*, and *Aspergillus flavus*	Rehman *et al*., 2015
19.	*Polyscias fulva*	ethyl acetate, n-butanol and residue showed activity against different *Candida* species and	Njateng *et al*., 2015

Raman, 1998). Most of the books describe classical procedures which pose limitations of reproducibility and quality. To ensure high quality herbal preparations, efforts are ongoing to replace traditional methodologies with modern sample preparation and extraction procedures. Classical methods are being complemented with modern techniques like microwave-assisted extraction, pressurized liquid extraction, matrix-assisted laser desorption/ionization mass spectrometry, and several others (Mukhtar et al. 2008).

Future Prospects

The importance of plants is becoming clear from the fact that more than 80% of the world population fulfills its medical needs from plants. There is a need of collaborative steps to make usage of medicinal plants common. The habitats which are rich in treasure of medicinal plants should be focused on. This would not only uplift the economy of the poor inhabitants, but also lead to preparation of medicines indigenously. The discovery of active principles from plants with the help of the developed world could also eliminate the emerging resistance of fungi to the synthetic drugs.

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