Plant-Derived Antifungal Agents: Past and Recent Developments

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Abstract

Fungal pathogens are increasing their vicinity and able to cause serious systemic and local infection in human beings. Although there are a few antifungal drugs available in the market, most of them are not completely safe and effective. On the other hand, plants have played an important role in the history of healthcare system. Several commonly available plant species belonging to algae, bryophytes, pteridophytes, and angiosperms are used in the treatment of fungal diseases by indigenous people and managed well the outburst of fungal diseases. Plant-based antimicrobials represent a vast untapped source of medicine, and they have enormous therapeutic potential as they can serve the purpose without any side effects that are often associated with synthetic antimicrobials. The present chapter deals with the historical background and the present status of medicinal plants used in the treatment of fungal diseases.

5.1 Introduction

5.1.1 Fungal Infections

Fungi are a large group with about 250,000 species available worldwide. Of which, more than 300 species have been reported as human pathogens (Guarro et al. 1997). The incidence of fungal infection has increased dramatically over the past few decades due to increase in the members of population susceptible to such infections.

The common systemic infections are aspergillosis, caused by species of *Aspergillus*, blastomycosis (*Blastomyces dermatitidis*); coccidioidomycosis, also called valley fever (*Coccidioides immitis*); cryptococcosis (*Cryptococcus neoformans*); histoplasmosis (*Histoplasma capsulatum*), candidiasis (*Candida* species); and *Pneumocystis* pneumonia (*Pneumocystis jirovecii* formerly known as *Pneumocystis carinii*). Superficial fungal infections include tinea capitis (*Microsporum canis*, *Trichophyton tonsurans*), tinea barbae (*T. rubrum*, *T. mentagrophytes*), tinea corporis (*M. canis*, *T. mentagrophytes*),

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tinea cruris (*T. rubrum*, *T. mentagrophytes*, *Epidermophyton floccosum*), tinea pedis (*T. rubrum*, *T. mentagrophytes*, *E. floccosum*), and tinea unguium (*T. rubrum*, *T. mentagrophytes*, *E. floccosum*). Approximately, 90 % of human fungal infections are caused by the species of *Aspergillus*, *Candida*, *Cladosporium*, *Epidermophyton*, *Microsporum*, and *Trichophyton* spp. Among these, aspergillosis and candidiasis have drawn more attention of scientists, policymakers, and medical epidemiologists.

Candida species are normal inhabitants of the skin, the gastrointestinal tract, the female genital tract, and urine. In contrast, molds produce conidia (spores) that are easily carried by wind and water, inhaled the floating spores through air, and cause sinus and lung infections. Sometimes the infection spreads to the brain and bones. Infections usually occur as a result of a decrease in natural human defenses or exposure to heavy fungal spores. Many infections are confined between the toes and a few spread over the skin. The internal infections become severe, if not taken care of in the initial stage and may cause permanent damage or even death. Therefore, the fungal infections are gaining prime importance in the healthcare system (Beck-Sague and Jarvis 1993). The increase in microbial infection in human beings and emergence of resistance in pathogen are the serious problems. The use of antimicrobial drugs for prophylactic or therapeutic purposes or for agricultural purposes has provided selective pressure favoring the survival and spread of resistant organisms. To overcome this, scientists are engaged in the development of new strategies to inhibit the fungal growth. Although a number of antifungal drugs are available in the market, many are proved to have serious side effects and hence, there is a great need of continuous search for newer, safer and cheaper antifungal agents from natural sources.

5.1.2 History of Plant Based Drug

There are about 250,000–500,000 species of plants on Earth (Borris 1996), and relatively a small group (1–10 %) of these is used as food by both humans and other animal species. Plants, in particular, have formed the basis of sophisticated traditional medicine systems with the earliest records dating from around 2600 BCE in Mesopotamia. About 1,000 plant-derived substances including oils of *Cedrus* species (cedar) and *Cupressus sempervirens* (cypress), *Glycyrrhiza glabra* (licorice), *Commiphora* species (myrrh), and *Papaver somniferum* (poppy juice) are documented and found useful even today. The best known record of Egyptian medicine is the "Ebers Papyrus" (1500 BCE), documented over 700 drugs of plant origin (Borchardt 2002). The Chinese materia medica reveals hundreds of important drugs starting from the first record dating from about 1100 BC to 659 AD (Huang 1999). Similarly, the Indian Ayurvedic system dates from before 1000 BC. Charaka and Sushruta Samhita reveal about 341 and 516 drugs, respectively (Dev 1999). Hippocrates in the late fifth century BC mentioned about 300–400 medicinal plants (Schuster 1966). Dioscorides, a Greek physician (100 CE), recorded the methods of collection, storage, and use of medicinal herbs during his travels with Roman armies. Galen (130–200 CE.), a practitioner and teacher of pharmacy and medicine in Rome, is well known for his complex herbal drug prescriptions. The Arabs, however, preserved much of the Greco-Roman expertise of the fifth to twelfth centuries and expanded it to include the use of their own resources along with Chinese and Indian herbs unknown to them.

Herbal drug systems are developed regionally in different parts of the world (Behl and Srivastava 2002), largely used in India and China (Xu 2004). In Europe and USA, the use of herbs declined due to the availability of purified and synthetic chemical drugs. In recent years, there has been a resurgence of the use of herbal drug as the side effects of chemical drugs became apparent and a call for green revolution and return to organic products.

5.1.3 Ethnomedicine

Ethnomedicine is practiced by various ethnic groups, especially by indigenous peoples. The word ethnomedicine is sometimes used as a synonym for traditional medicine. Ethnomedicine is

rather old and dates back to the time when the early man became conscious of his environment. Ethnomedicine helped in the survival of ancestors and has given knowledge about medicinal plants and its uses. Cultural man struggled for his existence as a hunter-gatherer and, with his trial-and-error experience, must have learned to distinguish useful and harmful plants, particularly the plants with healing properties (Weideman 2005). The earliest record of human civilizations reveals that the elders and wise men of those times used herbal medicines to treat various diseases. Information regarding these medicinal herbs is available in the old literature, folklore, mythological stories, epic poems, medical treatises, and old manuscripts, on palm leaves and copper plates and other records preserved even today (Weideman 2005).

5.1.4 Potential of Herbal Remedies as a Source of New Drugs

Plants have played an important role in the healthcare system across the world. Their role in the development of new drugs could be by serving either as a natural blueprint for the development of new drugs or as a phytomedicine to be used for the treatment of disease. It is estimated that plant materials have provided the models for 50 % of the modern drugs. Many commercially available modern drugs were initially used in crude form in traditional or folk healing practice (Dagne 1996). Since the beginning of the nineteenth century, a large number of biologically active secondary metabolites of plant origin have been found to have commercial application as drugs. Recently, there has been an upsurge of interest in the use of plants with folkloric reputations as sources of potentially useful compounds (Mourice et al. 1999). Analysis of the number and sources of anticancer and anti-infective agents, reported from 1984 to 1995, indicates that over 60 % of the approved drugs and pre-NDA (New Drug Application) candidates are of natural origin. A recent review reported that at least 119 compounds of plant origin are used currently, and 77 % of these are being derived from traditional medicinal plants (Douglas 1987). Several new small molecules of natural product-derived drugs have been introduced into therapy in various countries in recent years, including acarbose, artemether, capsaicin, docetaxel, dronabinol, galantamine, irinotecan, paclitaxel, tacrolimus, and topotecan. This trend is likely to continue in the future, at least for the treatment of disease states such as cancer and infectious diseases. In a recent statistical survey, it was pointed out that the origin of 30,000 bioactive natural products could be divided between animals (13 %), bacteria (33 %), fungi (26 %), and higher plants (27 %) (Ernst 1999). Despite the rapid development in the field of chemistry of medicinal research, many plant-derived drugs such as, atropine, resperine, morphine, cocaine, ergotamine, and digitalis still cannot be synthetically produced (Ernavitha 2008). Thus, the isolation of drugs from plants still holds good.

Plant-based antimicrobials represent a vast untapped source of medicine, and they have enormous therapeutic potential as they can serve the purpose without any side effects that are often associated with synthetic antimicrobials. First scientific studies on the antimicrobial properties of plant drugs were recorded in the late nineteenth century (Zaika 1975). Since then, several plants have been identified with potential antifungal properties and used in the treatment of fungal diseases.

5.1.5 Algae as an Antifungal Agents

Algae are a large and diverse group of plants which ranges from unicellular to multicellular forms. Blue-green algae, green algae, red algae, brown algae, and marine algae are known for their food and medicinal properties. Algae have also been used in the preparation of biodiesel, bioethanol, biobutanol, and hydrogen gases (Raja et al. 2013) and could be used as antioxidants, antibiotics, and virostatic agents. The most powerful water-soluble antioxidants such as polyphenols, phycobiliproteins, and vitamins are found in algae (Plaza et al. 2008). These antioxidants are able to prevent the occurrence of cancer cell formation (Richardson 1993). Marine algae have been used as food and medicine for centuries. They produce a wide spectrum of biological activities such as

antimicrobial (Bouhlal et al. 2011), antiviral (Kim and Karadeniz 2011), antifungal (De Felício et al. 2010), anti-allergic (Na et al. 2005), anticoagulant (Dayong et al. 2008), anticancer (Kim and Karadeniz 2011), antifouling, and antioxidant activities (Devi et al. 2011). The marine species such as *Rhodomela confervoides*, *Ulva lactuca*, *Cystoseira tamariscifolia*, and *Padina pavonica* from Bejaia coast are reported to have antifungal activity against *Aspergillus niger* (939 N), *Candida albicans* (ATCC 1024), and *Mucor ramaniannus* (NRRL1829). The extracts of *P. pavonica*, *R. confervoides*, and *U. lactuca* were very efficient against *M. ramaniannus* and *C. albicans* (Saidani et al. 2012). In another study (Tuney et al. 2006), the ethanolic extract of *P. pavonica* was active against *C. albicans*. In *Acanthaphora spicifera*, the methanolic extract showed higher antibacterial and antifungal activity against *E. coli*, *B. subtilis*, *Bacillus palmitus*, *P. aeruginosa*, and *C. albicans*, *M. gypseum*, and *A. niger* (Pandian et al. 2011). The purified carotenoid and chlorophyll pigments from *Chlorococcum humicola* (green alga) were effective against the harmful pathogens such as *E. coli*, *P. aeruginosa*, *Salmonella typhimurium*, *Klebsiella pneumoniae*, *V. cholera*, *S. aureus*, *B. subtilis*, *C. albicans*, *A. niger*, and *A. flavus* with a maximum of 80 % inhibition in benzene and ethyl acetate extracts (Bhagavathy et al. 2011). A report from Brazil reveals the chloroform and hexane fractions of *H. musciformis* inhibitory against *T. rubrum*, *T. tonsurans*, *T. mentagrophytes*, *M. canis*, *M. gypseum*, *C. albicans*, *C. krusei*, *C. guilliermondii*, and *C. parapsilosis*. The apolar extracts obtained from algae showed the best activity against pathogenic fungi (Guedes et al. 2012). *Asparagopsis taxiformis* (red alga) from Italy was found antifungal against *A. fumigatus*, *A. terreus*, and *A. flavus* with minimum inhibitory concentrations between <0.15 and >5 mg ml^{-1} against *Aspergillus* spp. Agar diffusion assays confirmed antifungal activity of *A. taxiformis* extracts against *Aspergillus* species (Genovese et al. 2013). Another red alga *Gracilaria arcuata* from Chabahar coasts showed very strong antibacterial and antifungal properties (Javad et al. 2014). *G. changii* is predominant in the mangrove areas and widely used in the traditional medicine in Malaysia. People in Malaysia use agar extracted from *Gracilaria* internally for coughs (Burkill 1935). Besides, *Gracilaria* sp. is boiled in vinegar and used to treat swollen knees and unhealthy sores (Burkill 1935). The methanol extract of *G. changii* exhibits inhibitory effect against candidiasis (Sasidharan et al. 2007). In Turkey, among the marine species such as *Cladophora glomerata*, *Enteromorpha linza*, *U. rigida*, *Cystoseira barbata*, *Padina pavonica*, *Corallina officinalis*, and *Ceramium ciliatum* studied from the coast of Vona, *Enteromorpha linza* and *P. pavonica* showed highest antifungal activity against *A. niger*, while *C. glomerata* showed highest antibacterial activity against *S. aureus* (Erturk and Tas 2011).

5.1.6 Bryophytes as Antifungal Agents

The bryophytes are a diverse group of land plants usually colonize in moist conditions. Alternation of generation with dominant free-living haploid gametophytic generation is an important feature of this group (Wyatt 1982). Bryophytes represent the simplest land plant group that are phylogenetically very old (Frahm 1994) and represent the level of evolution associated with transmigration to the land (Miller 1982). The secondary metabolites have provided numerous leads for the development of drugs, but the discovery of new drugs with novel structures has declined in the past few years. Bryophytes almost remain untouched in the drug discovery process. They are known to have numerous potential compounds, but much work remains to link medical effects with specific bryophyte species or compounds (Pant and Tewari 1990). Studies of their secondary metabolites are recent but reveal some original compounds, which have not seen even in higher plants. Mosses were traditionally used as antimicrobial agents in India (Frahm 2001) and as natural diapers (Ando and Mastuo 1984).

Bryophyte species actually produce broad-range antibiotics. Their usage in surgical dressings, diapers, and other human medicinal applications is well known not only in Asia (Frahm 2004) but also in Brazil (Pinheiro da Silva et al. 1989), England (Wren 1956), and Germany (Frahm 2004).

Chinese, Indians, and Native Americans have included bryophytes in their herbal medicine. Native Americans have used them for drugs, fibers, and clothing (University of Michigan, Dearborn 2003). Based on the concept of the doctrine of signatures, a variety of bryophytes, especially liverworts were used as herbal medicine (*Riccia* spp.), in the Himalayas to treat ringworm. Another study on *Riccia fluitans* from Florida indicated no ability to inhibit growth of *P. aeruginosa*, *S. aureus*, and *C. albicans* (Pates and Madsen 1955) including ringworm pathogen. The Gosiute native peoples in the USA use *Bryum*, *Mnium*, and *Philonotis* paste to reduce the pain of burns, bruises, and wounds (Flowers 1957). Similarly, the mixture of liverworts like *Conocephalum conicum* and *Marchantia polymorpha* thalli with vegetable oils is used in China for the treatment of bites, boils, burns, cuts, eczema, and wounds (Wu 1977; Ding 1982; Ando 1983). Indians in the Himalayan region use *M. polymorpha* or *M. palmata* to treat boils and abscesses as the young archegoniophore resembles a boil when it emerges from the thallus (Pant and Tewari 1989). The alcohol extract of *P. lyellii* was reported to be more active against *A. niger*, *A. fumigatus*, *F. oxysporum*, and *C. albicans*. *A. fumigates* was found to be more susceptible at 80 ng/disk concentration, and complete mycelial growth inhibition was seen at 1 mg/ml concentration which is better than ketoconazole (Subhisha and Subramoniam 2005). *Philonotis marchica*, *Grimmia pulvinata*, *Plagiomnium rugicum*, *Haplocladium* sp., *Bryum pallens*, *Drepanocladus aduncus*, *Pellia epiphylla*, and *Dumortiera hirsuta* were also found to have a broad spectrum of *antifungal* activity with maximum in ethanol extract (Shizadiann et al. 2009).

The antifungal compounds were also isolated from the liverwort *Plagiochila fasciculata* of New Zealand (Lorimer and Perry 1993, 1994). Scientists have found innumerable kinds of biological activity in compounds from bryophytes. Even in a single species, one might find multiple kinds of activity. For example, the liverworts *Plagiochasma japonica* and *Marchantia tosana* exhibit antitumor activity, antifungal and antimicrobial activity, inhibition of superoxide release, inhibition of thrombin activity, and muscle relaxation (Lahlou et al. 2000). One indication of the presence of unique and potential pharmaceutically important chemicals in bryophytes is the presence of unique odors especially in liverworts *Leptolejeunea* and *Moerckia* (Schuster 1966). *Lophozia bicrenata* has a pleasant odor, species of *Solenostoma* smell like carrots, *Geocalyx graveolens* has a turpentine-like odor, and *Conocephalum conicum* smells like mushrooms. The tropical *Plagiochila rutilans* smells like peppermint, due to the presence of several monoterpenoids (Heinrichs et al. 2001).

Although mosses are known to harbor fungi and will quickly become infected if kept moist in a plastic bag, some fungi are inhibited by many species of bryophytes, including many that cause skin infections. Jennings (1926) reported moss immunity to molds as early as 1926, but the possibility of using them as a source of antifungal activity seems to have been largely overlooked. Among these, *Hypnum cupressiforme* has remarkable antibacterial and antifungal effects. The absence of fungal diseases in liverworts led Pryce (1972) to suggest that lunularic acid, an aging hormone found in liverworts but not in mosses, might be responsible for liverwort antifungal activity. The degree of antibiotic activity in a given species may depend on the age of the gametophyte (Banerjee and Sen 1979), and this is well supported by the age-dependent antifungal activity in liverwort *Herbertus aduncus* against *Botrytis cinerea*, *Pythium debaryanum*, and *Rhizoctonia solani*. They subsequently isolated three aging substances, namely, alpha-herbertenol, beta-herbertenol, and alpha-formylherbertenol from it (Matsuo et al. 1982a, b, 1983). The paste of *Ceratodon purpureus* and *Bryum argenteum* to cure fungal infections of horses (Frahm 2004) was used by industrious horse owners and cured the fungal infections in horses within 24 h. The cinnamolide, the active compounds from *Porella* and *Makinoa*, showed antidermatophytic activity, and *Dumortiera hirsuta*, *Sphagnum portoricense*, and *Orthotrichum rupestre* showed antifungal activity against *C. albicans* (Subramoniam and Subhisha 2005a; Mc Cleary and Walkington 1966). A group of phenolic compounds isolated from liverwort have shown potent activity as an

antifungal, antioxidant, and anticancer agent (Dai and Sun 2008), while plagiochin E from *Marchantia polymorpha* could reverse fungal resistance to fluconazole and induce apoptosis in *C. albicans*. Riccardin D from *Dumortiera hirsuta* inhibits hyphal formation and interferes with biofilm formation. Among the bisbibenzyls extracted from liverworts, isoriccardin C and BS-34 found better antifungal compounds in a dose-dependent manner (Sun 2009).

5.1.7 Pteridophytes as Antifungal Agents

The pteridophytes are an important group of plants that constitutes ferns and their allies. There are over 250 different genera and 12,000 species of ferns reported all over the world (Chang et al. 2011). Of these, between 2,200 and 2,600 species occur in China accounting about 22 % of the world total. Out of 1,250 species in India, 173 species are used as food, flavor, dye, medicine, bio-fertilizers, oil, fiber, and biogas producer (Manickam and Irudayaraj 1992). The secondary metabolites like alkaloids, glycosides, flavonoids, terpenoids, sterols, phenols, sesquiterpenes, etc., are important components in fern and are used in various industries (Kulandairaj and Britto 2000). Kirtikar et al. (1935) have described 27 species, Nayar (1959) 29 species, Chopra et al. (1956) 44 species, and Nadkarni (1954) 11 species of pteridophytes having medicinal importance. A detailed review on the medicinal uses of 105 ferns is published by May (1978). On the basis of phytochemical, pharmacological, and ethnobotanical studies, Singh (1999) reported 160 useful pteridophytes in India. *Selaginella bryopteris* (Linn.) Bak. is considered as a highly useful plant for unconsciousness condition, *Equisetum arvense* Linn. is used in nasal polyps and kidney infections and its ashes are useful in acidity, *E. debile* Roxb. is diuretic and given in gonorrhea, *Lycopodium clavatum* Linn. in the form of decoction is used in rheumatism and diseases of the lung and kidney, the leaf paste of *Ophioglossum reticulatum* Linn. is used in headache, *Botrychium virginianum* Sw. is used in dysentery, *Helminthostachys zeylanica* (Linn.) Hook. is used to revert impotency and also used as a brain tonic, and *Lygodium flexuosum* (Linn.) Sw. is an expectorant and also used in the treatment of ulcers, cut wounds, and sprains. The fronds of gleicheniaceous fern *Dicranopteris linearis* (Burm.) are used in the treatment of asthma and sterility in women, and *Osmunda regalis* Linn., the "royal fern," is used as a styptic and tonic, while the rhizome of *Angiopteris evecta* (Forst.) Hoffm. is used for scabies (Vasudev 1999). As per ancient literature, the pteridophytes have been known for about 2,000 years (Kirtikar and Basu 1975) and are used as medicine in Ayurvedic and Unani systems of medicine (Uddin et al. 1998). The antimicrobial potential of some ferns has been studied by Kumar and Kaushik (1999) and Parihar and Bohra (2002a, 2003). The paste of *Adiantum incisum* Forsk. and *A. venustum* is useful in the healing of wounds (Samant et al. 1998; Kholia and Punetha 2005).

The edible Malaysian fern species like *Stenochlaena palustris*, *Diplazium esculentum*, *Nephrolepis biserrata*, and *Acrostichum aureum* were screened against *A. niger*, *Rhizopus stolonifer*, and *C. albicans*, and a broad spectrum of antifungal activity was found in *Diplazium esculentum* leaves. The study shows that the fern extracts are favorable antifungal agents with potential applications in public heath against fungal diseases (Zakaria and Sanduran 2010). *Hemionitis arifolia* (Burm. f.) Moore., *Pteridium aquilinum* (Linn.) Kuhn., and *Christella parasitica* (Linn.) H. Lev. were evaluated against the fungal pathogens *Puccinia arachidis* and *Phaeoisariopsis personata* causing rust and early leaf spot diseases in groundnut, respectively, which are the pathogens sensitive to all three fern extracts. The chloroform extract of *H. arifolia* was found to have maximum antifungal activity against both fungi (Kitherian Sahayaraj et al. 2009). The aqueous and ethanolic frond extracts of *Cheilanthes anceps* were proved to be effective against *A. flavus* and *A. niger* (Mishra and Verma 2009). The Bheel tribe in Mt. Abu area use leaf juice of *Adiantum incisum* for the treatment of skin disease; however, in Goram Ghat area, the leaf powder mixed with butter is used for controlling

internal burning in the body (Parihar and Parihar 2006). The phenolic compounds are abundantly present in lycopodiophyta (Pedersen and Ollgaard 1982), pteridophyta, angiosperm, and gymnosperm (Carnachan and Harris 2000). Ferns in particular serve as an important source of some phenolic compounds such as kaempferol, which is known to be extracted from *Phegopteris connectilis* (Adam 1999), and kaempferol-3-O-rutinoside, extracted from *Selliguea feei* (Baek et al. 1994). *Salvinia molesta*, a freshwater fern, is a good source of phenolics such as hypogallic acid, caffeic acid, paeoniflorin, and pikuroside (Choudhary et al. 2008).

Ethnomedicinally, *Adiantum* Linn. is an important plant popularly known as "Hansraj" in Ayurvedic System of Medicine and is used in the treatment of cold; tumors of the spleen, liver, and other viscera; skin diseases; bronchitis; and inflammatory diseases. Meenakshi Singh et al. (Jan 2008) have studies the antimicrobial property of four important species, i.e., *Adiantum capillus-veneris*, *Adiantum peruvianum*, *Adiantum venustum*, and *Adiantum caudatum*, against five gram-positive and six gram-negative bacteria (including multiresistant *S. aureus*) and eight fungal strains. The maximum activity was exhibited by the methanolic extract of *A. venustum* followed by *A. capillus-veneris*, *A. peruvianum*, and *A. caudatum*. *Pityrogramma* is a genus with about 17 species occurring mainly in tropical America (Smith et al. 2006). The ethanolic extract of *Pityrogramma calomelanos* (L.) Link showed good activity against *S. aureus* when associated with aminoglycosides and against species of *Candida* with benzoilmetronidazol. The results indicated that *P. calomelanos* should be studied as a possible source of natural products to combat bacteria and fungi either directly or by modulating the mechanisms of resistance of these microorganisms and enhancing the antimicrobial activity of these drugs (Souza et al. 2012). *Stenochlaena palustris* leaf extract tested for its fungicidal activity was found effective against food-borne pathogen *A. niger*. Morphological changes in *A. niger* treated with the fern leaf extract were observed through scanning electron microscope which reveal cell wall disruption with flattened appearance on hyphae (Sumathi and Parvathi 2010). Ethanol and methanol extracts of *Drynaria quercifolia* (L.) J. Smith rhizomes were also found to be inhibitory against *C. albicans* and *Cryptococcus neoformans*. Saponin, coumarin, and terpenoids were detected in ethanol extract and showed greater antibacterial and antifungal activity than methanol extract (Pargavi and Shivakumar 2014).

5.1.8 Higher Plants as Antifungal Agents

Herbal therapy for skin disorders has been used for thousands of years. Even our biologically close relatives, the great apes, use herbal self-medication (Huffman 2001). Specific herbs and their uses developed regionally, based on locally available plants and through trade in ethnobotanical remedies. The great importance of flowering plants in developing new therapeutic tools is evident. Medicinal plants and their derivatives are important for pharmacological research and drug development.

The natural products can be used directly as therapeutic agents, or as a source of raw materials for synthesis of new pharmacologically active models (Brazil 2006). In Chinese medicine, *Psoralea corylifolia* and *Eucalyptus globulus* have been used in the treatment of dermatomycosis caused by *T. mentagrophytes* and *T. rubrum* (Lau et al. 2010). The antifungal activity of *Eugenia umbelliflora* Berg. (Machado et al. 2009) against *E. floccosum*, *T. mentagrophytes*, *T. rubrum*, *M. canis*, and *M. gypseum* and *Wrightia tinctoria* against *T. rubrum*, *E. floccosum*, *A. niger*, and *Scopulariopsis brevicaulis* was reported (Ponnusamy et al. 2010). The major compound, identified as indirubin, is inhibitory against dermatophytes such as *E. floccosum*, *T. rubrum*, *T. tonsurans*, *T. mentagrophytes*, and *T. simii*. It was also active against *A. niger*, *C. albicans*, and *Cryptococcus* sp. (Newman and Cragg 2007). Lima et al. (2011) reported antifungal activity

of the essential oils (EOs) of *Gymnophyton polycephalum*, *Satureja parvifolia*, and *Lippia integrifolia* against *M. gypseum*, *T. mentagrophytes*, and *T. rubrum*. The originality of many structures of natural products attracts attention to their use as a starting point for semi-synthesis and total synthesis (Butler 2005). The development of chemotherapeutic agents of synthetic origin and the discovery of powerful new antimicrobials isolated from natural sources account for invaluable contributions in the fight against fungal resistance (Silveira et al. 2006). The extracts obtained from plants such as *Euphorbia prostrata*, *Salvia texana*, *Colubrina greggii*, and *Clematis drummondii* have shown promising results for stimulating the search for new potential antifungal plant sources (Alanís-Garza et al. 2007).

Antifungal activity of *Indigofera suffruticosa* was effective against *T. rubrum* and *M. canis* (Sonia Periera et al. 2006). The oils of *Ocimum gratissimum* and *Trachyspermum ammi* exhibited strong antidermatophytic properties (Tiwari et al. 2003). Ranganathan (1996) reported the MIC of neem seed extract was lower than that of the neem leaf when tested against different species of *Trichophyton* and *Epidermophyton floccosum*. The MIC (31 μg/ml) of neem seed extract was also determined by Natarajan et al. (2003) against dermatophytes. The concentration at 15 μg/ml (below MIC) was observed to be sufficient for distorting the growth pattern of the organisms. In another study, the ethanolic extract at 100 μg/ml concentration was more active against dermatophytes (Pankajalakshmi 1994). The flower extract of *Tagetes erecta* showed maximum antimycotic activity against *F. oxysporum* and *T. mentagrophytes* followed by whole plant of *T. patula* and leaf extract of *T. erecta* (Rai and Acharya 1999). The *Capparis spinosa* and *Juglans regia* inhibited the growth of *M. canis*, *T. violaceum*, and *T. mentagrophytes* (Ali-Shtayeh and Abu Ghdeib 1999). *Nelumbo nucifera* rhizome extract was inhibitory against yeast (Mukherjee et al. 1995), and *Cinnamomum tamala* and while *Citrus maxima* oil exhibited complete inhibition of mycelial growth of *T. mentagrophytes* and *M. audouinii* (Dubey et al. 1998). *Wrightia tinctoria* leaves also possessed potent antimicrobial properties against dermatophytes. The methanol and ethanol extracts were found effective against bacteria and hexane extract against dermatophytes suggesting that the active principles may be useful in the topical treatment of superficial skin infections (Kannan et al. 2006).

Turmeric oil isolated from *Curcuma longa* L. by Apisariyakul et al. (1995) was inhibitory against 15 isolates of dermatophytes at 1:40–1:320 dilutions. A wide range of inhibition zone from 6.1 to 26.0 mm against 29 clinical strains of dermatophytes was reported by Mansuang et al. (2002) using crude ethanol extract of *Curcuma longa*. The antifungal activity of essential oils of higher plants against ringworm caused by *T. mentagrophytes* and *M. audouinii* was reported by Yadav and Dubey (1994). *Cinnamomum tamala*, *Citrus maxima*, *Cymbopogon citratus*, *Eucalyptus citriodora*, *Eupatorium cannabinum*, *Nepeta hindostana*, and *Ocimum canum* oils were absolutely toxic against both the test fungi. The essential oil from the fruits of *Luvunga scandens* was found very good against dermal infections (Garg and Jain 1999). In recent years, these reports have involved mainly the members of Lamiaceae and Asteraceae families. The antifungal effects of essential oils from several species of the Lamiaceae family, viz., *Satureja montana* L., *Lavandula angustifolia* Mill (D'Auria et al. 2005), *Lavandula hybrida* Reverchon, *Origanum vulgare* L., *Rosmarinus officinalis* L., and six chemotypes of *Thymus vulgaris* L., were studied against *C. albicans*. The greatest efficiency was obtained with the essential oil from *T. vulgaris*. An extensive study has been carried out on the antifungal activity of the essential oils from *Lavandula* and *Rosmarinus*. The essential oil from *Hyptis ovalifolia* leaves was found very effective against dermatophytes at a concentration of $<$500 μg/ml (eSouza et al. 2002).

In the Liliaceae family, reports on the antifungal activity concern mainly the *Allium* genus. By using an agar dilution assay, the antifungal activity of aqueous extracts prepared from *Allium cepa* L. and *Allium sativum* L. was evaluated against *Malassezia furfur*, *C. albicans*, as well

as several strains of various dermatophyte species by Shams et al. (2006). The results indicate that onion and garlic might be promising sources of drugs for the treatment of fungal diseases caused by *Candida*, *Malassezia*, and the dermatophytes. Similar studies on the antifungal activity of onion and garlic were reported by Ghahfarokhia et al. (2004) against *T. rubrum* and *T. mentagrophytes*. According to Karunyal Samuel et al. (2001), 200 mg/ml concentration of *Allium sativum* aqueous bulb extract is effective against *T. rubrum*. Pyun. Shin (2006) studied the activity of essential oils from *Allium fistulosum* L., *A. sativum*, and *A. cepa* (Liliaceae) against three species of *Trichophyton* and found *A. sativum* oil as the strongest growth inhibitor against *T. rubrum*. There have been a large number of antifungal screening programs being carried out in plant drugs used in traditional medicine of Eastern Europe and Africa. Tadeg et al. (2005) screened the traditionally used Ethiopian medicinal plants, namely, *Acokanthera schimperi*, *Calpurnia aurea*, *Kalanchoe petitiana*, *Lippia adoensis*, *Malva parviflora*, *Olinia rochetiana*, *Phytolacca dodecandra*, and *Verbuscum sinaiticum*, against fungal pathogens and reported *L. adoensis* and *O. rochetiana* to be the effective antifungal plant drugs. Similarly, in the traditional practices in Southern Brazil, the aerial parts of *Pterocaulon alopecuroides* and *Pterocaulon polystachyum* are used to treat mycoses. In vitro studies indicated the crude methanol extract of *P. polystachyum* as the most active one for mycoses (Stein et al. 2005). In other studies, Lamidi et al. (2005) evaluated 77 crude extracts from leaves and stem barks of 15 Gabonese plants used in traditional medicine as antifungal agents and revealed ethanol extract of *Polyalthia suaveolens* as a good antifungal agent effective at 1 mg/ml concentration. From Balochistan, Pakistan, Zaidi and Crow (2005) reported very good antifungal activity in *Zygophyllum fabago* L. and *Vincetoxicum stocksii* against *C. albicans*.

Nigella sativa L. (Aljabre et al. 2005), *Melaleuca alternifolia* oil (Hammer et al. 2002), flowers of *Yucca gloriosa* L. (Favel et al. 2005), *Boerhavia diffusa* L. (Agrawal and Rangari 2003), *Hypericum* growing in Southern Brazil (Fenner et al. 2005), *Gentianella nitida* Griseb. (Rojas et al. 2004), *Croton urucurana* Baill. bark (Gurgel et al. 2005), *Inula viscosa* (Maoz and Neeman 1998), *Piper guineense* (Ngono Ngane et al. 2003), *Chimaphila umbellate* (Isabel et al. 2008), *Hypoestes serpens* (Rasoamiaranjanahary et al. 2003) and *Mitracarpus villosus* leaves (Irobi and Daramola 1993) were reported to have antifungal property. Similarly, the essential oils from *Cymbopogon citratus* (Lachoria et al. 2000); *Allium fistulosum* L., *A. sativum* L., and *A. cepa* L. (Pyun and Shin 2006); *Catharanthus roseus* (Singh and Singh,1997 and Rai and Upadhyay 1998); *Citrus sinensis* (Patra et al. 2003); *Syzygium aromaticum* L. (Merr. and Perry) (Taguchi et al. 2005); *Eucalyptus globulus* Labill., *Eucalyptus maculata* Hook., and *Eucalyptus viminalis* Labill. (Takahashi et al. 2004); *Eucalyptus rostrata* (Singh et al. 1988); *Satureja montana* L., *Lavandula angustifolia*, *L. hybrida* Reverchon, *Origanum vulgare* L., *Rosmarinus officinalis* L., and *Thymus vulgaris* L. (Tarfa et al. 2004); *Chrysactinia mexicana* Gray. (Cardenas et al. 2005); *Azadirachta indica* (Pant et al. 1986; Vaijayanthimala et al. 2004); *Cassia alata* (Ibrahim and Osman 1995); *C. fistula* (Lillykutty and Santhakumari 1969); mint (Kishore et al. 1993); *Artemisia herba-alba* and *A. judaica* (Charchari et al. 1996); *Acalypha indica* (Gopalakrishnan et al. 2000); *Acalypha wilkesiana* (Alade and Irobi 1993); *Calendula officinalis* (Kasiram et al. 2000); *Salvia mirzayanii* Rech. F. and Esfand. (Portillo et al. 2005); *Solanum dulcamara* (Kumar and Bhadauria 2009); *Ocimum* spp. (Janseen et al. 1989); *O. sanctum* (Gangrade et al. 1989); *Ocimum gratissimum* L. (Silva et al. 2005); *Lawsonia inermis* (Bhakuni et al. 1971; Bhatnagar et al. 1961; Misra and Dixt 1979); *Psoralea corylifolia* (Sharma and Singh 1979; Grover and Rao 1979; Gupta et al. 1962); *Curcuma longa* rhizome (Vaijayanthimala et al. 2004); *Pongamia pinnata* seed oil (Kesari et al. 2010); and lemon and lantana (Jain et al. 2004) were reported to have antifungal activity. The effective antifungal compounds isolated from different medicinal plants against pathogenic fungi are given in Tables 5.1 and 5.2.

Table 5.1 Plant-derived antifungal compounds from different plant parts

Sl. no	Name of the plant	Part used	Active compounds	Name of the compound class	Targeted microorganism studied	Ref. no.
1	*Aesculus pavia* L., Sapindaceae	Leaves	S-6-[2-(Hydroxy methyl) butoxy]-7-hydroxy-4-methyl-2H-chromen-2-one, named Pavietin	Prenylated coumarin	*Guignardia aesculi*	Curir et al. (2007)
2	*Ailanthus excelsa* Roxb., Simaroubaceae	Stem bark	Methanol extract of the plant was partitioned with chloroform	Extract	*A. niger*, *A. fumigatus*, *Penicillium frequentans*, *P. notatum*, *Botrytis cinerea*	Deepa et al. (2004)
3	*Ajania fruticulosa* (Ledeb.) Poljak, Asteraceae	Aerial parts	(I) 1E,2E-Epoxy-3E,4D,8E,10D-titrahydroxyguaia-11(13)en-12-Olide	Guaianolides	*Candida albicans*	Meng et al. (2001)
			(II) 1E,2E-Epoxy-3E,4D,9D,10D-tetrahydroxyguaia-11(13)-en-12,6D-olide			
			(III) 1E,2E-Epoxy-10D-hydroperoxy-3E,4D,8E-trihydroxyguaia-11(13)-en-12,6D-olide			
4	*Asterella angusta* (Steph.), Pandé et al., Aytoniaceae		Asterelin A, asterelin B, 11-O-demethyl marchantin, dihydroptychantol A	Bis(benzyl)	*C. albicans*	Qu et al. (2007)
5	*Azadirachta indica* A. Juss., Meliaceae	Green leaves	Nimonol, isomoldenin	Limonoids		Suresh et al. 1997
6	*Ballota glandulosissima*	Aerial part	Kumatakenin, pachypodol, 5-hydroxy-7,3′,4′-trimethoxy, flavone, velutin, retusin	Flavonoids	*C. albicans*, *C. krusei*, *C. glabrata*	Citoglu et al. (2003)
7	*Bridelia retusa* (Linn.) Spreng., Euphorbiaceae	Stem bark	(E)-4-(1,5,Dimethyl-3-oxo-1-hexenyl) benzoic acid	Bisabolane sesquiterpenes	*Cladosporium cladosporioides*	Jayasinghe et al. 2003
8	*Calophyllum Caledonicum* Vieill. ex Planch. and Triana, Clusiaceae	Stem bark	Caledonixanthone E	Xanthone	*A. fumigatus*	Larcher et al. (2004)
9	*Centaurea*, Asteraceae		(+) Enicin, salonitenolide, (+) costunolide, (−) dehydro-custuslactone, lychnopholideermantholide C	Sesquiterpene lactones	*Cunninghamella echinulata*	Barrero et al. (2000)

10	*Chenopodium procerum* Hochst. ex Moq., Chenopodiaceae	Aerial part	Irilin A, irilin B, dihydrowogonin, pygmol	Isoflavone, flavanone, sesquiterpene	*Cladosporium cucumerinum*	Bergeron et al. (1995)
11	*Clematis tangutica* (Maxim.) Korsh., Ranunculaceae	Aerial parts	(1) 3-o-D-L-Arabinopyranosyl-hederagenin-28-0-D-L-rhamnopyranosyl ester	Terpene saponins	*Saccharomyces cerevisiae*	Du et al. (2003)
			(2) 3-0-E-D-Glucopyranosyl-(1o4)-D-L-arabinopyranosyl-hederagenin-28-o-D-L-rhamnopyranosyl ester			
12	*Clytostoma ramentaceum*		Ursolic acid, 2-(3,4-dihydroxophenyl) ethanol		*A. niger*, *F. oxysporum*	Lorimer and Perry (1994)
13	*Colutea arborescens* L., Fabaceae	Root bark	(1) Coluteol (3,5-dihydroxy-7,2,4-trimethoxyisoflavan)	Isoflavan, isoflavan quinone	*Saccharomyces cerevisiae*	Grosvenor and Gray David (1998)
			(2) Colutequinone B (7,4 6-trimethoxyisoflavan-2 5-quinone)			
14	*Commiphora wightii* (Arn.) Bhandari, Burseraceae		Muscanone	Flavanone	*C. albicans*	Fatope et al. (2003)
15	*Coptis japonica* (Thunb.) Makino, Ranunculaceae		Berberine	Alkaloid	*B. berengeriana*, *G. cingulata*, *P. expansum*	Chung and Paik (1997)
16	*Cordia alliodora* (Ruiz and Pav.) Oken, Boraginaceae	Root bark	(1) 1-(3-Methoxypropanoyl)-2,4,5-trimethoxy benzene	Phenylpropanoid derivative, prenylated hydroquinone	*Cladosporium cucumerinum*	Ioset et al. (2000)
			(2) 2-2(Z)-(3-Hydroxy-3-7-dimethylocta-2,6-dienyl)-1,4-benzenediol			
17	*Cryptomeria japonica* (L. f.) D. Don, Cupressaceae	Bark	12-Methoxy-6D,11-dihydroxyabieta-8,11,13-triene	Diterpenoids	*A. alternata*, *P. oryzae*, *R. solani*, *F. oxysporum*	Kofujita et al. (2006)
18	*Cuban propolis*		A novel polyisoprenylated benzophenone	Ketone	*C. albicans*, *C. tropicalis*	Rubio et al. (1999)
19	*Cudrania cochinchinensis* Lour., Moraceae	Roots	Cudraxanthones S	Xanthone 7	*Cryptococcus neoformans*, *A. fumigatus*, *A. nidulans*, *C. glabrata*	Fukai et al. (2003)
			(1) [1,3,5,6-Tetrahydroxy-2-(1,1-dimethyl-2-propanyl)xanthone]			
			(2) Toxyloxanthone			
			(3) Wightone			

(continued)

Table 5.1 (continued)

Sl. no	Name of the plant	Part used	Active compounds	Name of the compound class	Targeted microorganism studied	Ref. no.
20	*Delphinium denudatum* Wall., Ranunculaceae	Roots	8-Acetylheterophyllisine, vilmarrianone, panicutin	Diterpene, alkaloid, alkaloid	*Allescheria boydii*, *E. floccosum*, and *A. niger*, *A. boydii*, *Stachybotrys atra*, *Pleurotus ostreatus*	Rahman et al. (1997)
21	*Detarium microcarpum* Guill. and Perr., Leguminosae	Fruit pulp	(1) 3,4-Epoxyclerodan-13E-en-15-oic acid	Clerodane diterpenes	*Cladosporium cucumerinum*	Cavin et al. (2006)
			(2) 5D,8D-(2-Oxokolavenic acid)			
			(3) 4-Dihydroxyclerodan-1 3Z-en-15-oic acid			
22	*Eriosema tuberosum* Hochst., Leguminosae	Roots	Eriosemaone A, eriosemaone B, eriosemaone C, eriosemaone D, flemichin D	Polyphenols	*Cladosporium cucumerinum*, *C. albicans*	Ma et al. (1995)
23	*Eugenia dysenterica* DC., Myrtaceae	Leaves	E-Caryophyllene, D-humeelene, limonene, D-thujine	Sesquiterpenes, monoterpene hydrocarbon	*C. albicans*	Costa et al. (2000)
24	*Ferula diversivittata* Rgl. et Schmalh., Apiaceae	Roots	Diversolides A–G, diversolide E	Sesquiterpene, lactone derivative	Antifungal	Iranshahi et al. (2008)
25	*Ganoderma annulare* (Lloyd) Boedijn, Ganodermataceae		5D-ergost-7-en-3E-o1, applanoxidic acids A, C and F	Sterol, triterpenes	*Microsporum canis*, *T. mentagrophytes*	Smania et al. (2003)
26	*Garcinia mangostana*, Linn., Guttiferae	Fruit	Mangostin, 8-desoxygartanin, BR, xanthone, gartanin, beta-mangostin, garcinone-D	Xanthones	*F. oxysporum* f. sp. *vasinfectum*, *Alternaria tenuis*, *Drechslera oryzae*	Gopalakrishnan et al. (1997)
27	*Glaucium oxylobum* Boiss and Buhse, Papaveraceae	Aerial parts	Dicentrine, glaucine, protopine D, allocryptopine	Alkaloids	*M. gypseum*, *M. canis*, *T. mentagrophytes*, *Epidermophyton*, *Floccosum*	Morteza et al. (2003)
28	*Gmelina arborea* Roxb. Lamiaceae	Heartwood	Catalpol	Iridoid glycoside	*Trametes versicolor*	Kawamura and Ohara (2005)
29	*Guarea macrophylla* Vahl., Meliaceae		Caryophyllene oxide, guai-6-en-10E-ol	Sesquiterpenes	*C. cladosporioides*, *C. sphaerospermum*	Costa et al. (2000)
30	*Hildegardia barteri* (Mast.) Kosterm., Sterculiaceae	Root	Hilde gardiol, 2-hydroxy maackiain, farrerol	Isoflavan, flavonoid	*C. albicans*	Meragelman et al. (2005)

31	*Hypoestes serpens* (Vahl) R. Br. Acanthaceae	Leaves	Fusicoserpenol, dolabeserpenic acid	Diterpenes	*C. cucumerinum*, *C. albicans*	Rasoamiaranjanahary et al. (2003)
32	*Khaya senegalensis* (Desr.) A. Juss., Meliaceae	Fruits	Seneganolide A, 2-hydroxyseneganolide A, 2-acetoxyseneganolide A, two limonoids,	Limonoid	*Botrytis cinerea*	Abdelgaleil et al. (2004)
33	*Licania intrapetiolaria*, Chrysobalanaceae	Roots	Intrapetacin B	Clerodane diterpenoid	*A. niger*	Oberlies et al. (2001)
34	*Lycium chinense* Mill., Solanaceae	Roots, barks	Dihydro-N-caffeoyltyramine, trans-N-fereeloyloctopamine, trans-N-caffeoyltyramine, cis-N-caffeoyltyramine	Phenolic amides	*C. albicans*	Lee et al. (2004)
35	*Magnolia grandiflora* L., Magnoliaceae	Stem bark	Costunolide, 1,10 epoxyparthenolide	Sesquiterpene lactone	*Nigrospora* spp., *R. solani*, *Helminthosporium*, *Alternaria alternata*, *Fusarium culmorum*	Ahmed and Abdelgaleil (2005)
36	*Melicope borbonica* (Bory), Rutaceae	Leaves	Xanthoxylin, scoparone, limettin	Acetophenone coumarins	*C. albicans*, *Penicillium expansum*	Simonsen et al. (2004)
37	*Monnina obtusifolia* H. B. and K., Polygalaceae	Aerial parts	Two xanthones	Xanthone	*Trichophyton mentagrophytes*	Pinto et al. (1994)
38	*Nepeta clarkei* Hook. F., Lamiaceae	Aerial part	Actinidine	Terpene alkaloid	*A. flavus*	Saxena Jyoti and Mathela (1996)
39	*Nepeta leucophylla* Benth, Lamiaceae	Aerial part	Iridodial-E-monoenol acetate	Iridoid	*A. flavus*, *A. ochraceus*, *Penicillium citrinum*, *P. viridicatum*	Saxena Jyoti and Mathela (1996)
40	*Peperomia serpens* (*Sw.*) Loudon., Piperaceae	Leaves	Two chromenes	Chromene	*C. cladosporioides*, *C. sphaerospermum*	Li et al. (1999)
41	*Phyllanthus piscatorum* Kunth, Euphorbiaceae		Justicidin B	Arylnapthalide lignan	*A. fumigatus*, *A. flavus*, *C. albicans*	Gutierrez et al. (2002)
42	*Phytolacca tetramera* Hauman, Phytolaccaceae	Berries	Phytolaccoside B, phytolaccoside E	Monodesmosidic triterpenoid saponins	*Trichophyton mentagrophytes*	Kariba et al. (2002)
43	*Piper arboretum*, Piperaceae	Leaves	(1) N-[10-(13,14-Methylenedioxy-phenyl-7(E),9(Z)-pentadienoyl]-pyrolindine (2) Arboreumine	Amide	*Cladosporium sphaerospermum*	Sartori et al. (2003)

(continued)

Table 5.1 (continued)

Sl. no	Name of the plant	Part used	Active compounds	Name of the compound class	Targeted microorganism studied	Ref. no.
44	*Piper crassinervium*	Leaves	(1) 1,4-Dihydroxy-2-(3,7-dimethyl-1-oxo-2-E,6-octadienyl)benzene	Prenylated hydroquinone	*C. cladosporioides*, *C. sphaerospermum*	Cavin et al. (2006)
			(2) 1,4-Dihydroxy-2-(3,7-dimethyl-1′ oxo-2-Z,6-octadienyl)benzene			
			(3) 1,4-Dihydroxy-2(7-methyl-3-methylene-1-oxo-4,7-peroxide-octyl) benzene			
45	*Piper hispidum* Sw., Piperaceae	Leaves	N-[7-(3,4-Methylenedioxyphenyl)-2 (z),4(Z)-heptadienoyl] pyrrolidine	Pyrrolidine amide	*Cladosporium sphaerospermum*	Alecio et al. (1998)
46	*Piper hispidum* Sw., Piperaceae		Two new amides	Amide	*Cladosporium sphaerospermum*	Navickiene et al. (2000)
47	*Piper lanceaefolium* Kunth, Piperaceae	Leaves	Four new benzoic acid derivatives together with tabogenic acid, pinocembrin, and pinocembrin chalcone. Lanceaefolic acid methyl ester and pinocembrin chalcone	Benzoic acid derivative	*C. albicans*	Lopez et al. (2002)
48	*Piper umbellatum* Linn., Piperaceae	Branch	*Piper umbellatum* (A–D)	Alkaloids	*C. albicans*	Borris (1996)
49	*Piscidia erythrina* L., Fabaceae	Root bark	Isopiscerythrone, allolicosi flavone A, piscisoflavone A, piscisoflavone B	Isoflavones	*Cladosporium herbarum*	Monga and Mohapatra (1980)
50	*Plagiochila fasciculata* Lindenb., Plagiochilaceae		2-Hydroxy-4,6-dimethoxyacetophenone, 2-hydroxy-3,4,6-trimethoxyacetophenone	Acetophenone	*T. mentagrophytes*, *Cladosporium resinae*	Alecio et al. (1998)
51	*Pogostemon cablin* Benth, Lamiaceae	Whole plant	5-Hydroxy-7,3,4′-trimethoxyflavanone, 5-hydroxy-7,4-dimethoxyflavanone, 3,5-dihydroxy-7,4′-dimethoxyflavanone	Flavonoids		Cornet et al. (2002)
52	*Prismatomeris fragrans* Geddes, Rubiaceae	Roots and stem	Nordamnacanthal, damnacanthal	Anthraquinones	*C. albicans*	Saxena et al. (1996)
53	*Rudgea viburnoides* (Cham.) Benth., Rubiaceae	Ripe fruit	Viburgenin	Triterpene	*Cladosporium cladosporioides*	Claudia et al. (1998)
54	*Schizozygia coffaeoides* Baill., Apocynaceae	Leaves and roots	6,7-Dehydro-19E-hydroxy schizozygine	Alkaloid	*Cladosporium cladosporioides*	Kariba et al. (2002)

55	*Selaginella tamariscina* (Beauv.), Selaginellaceae	Whole plant	Amentoflavone	Biflavonoid	*C. albicans*	Jung et al. (2006)
56	*Smallanthus sonchifolius* (Poepp. and Endl.) H. Robinson, Asteraceae	Leaf extract	Sonchifolin	Melampolide	*Pyricularia oryzae*	Hashidoko et al. (1995)
57	*Smilax medica* Schltdl. and Cham. Smilacaceae	Roots	Two new steroidal saponins and the known disporoside A	Steroidal saponins	*C. albicans*, *C. glabrata*, *C. tropicalis*	Sauton et al. (2005)
58	*Sorocea muriculata* Miq., Moraceae	Root extract	Sorocenol H	Oxygen heterocyclic, Diels-Alder-type adduct	*C. albicans*, *Cryptococcus neoformans*, *A. fumigatus*	Samir et al. (2008)
59	*Spathodea campanulata* P. Beauv., Bignoniaceae	Roots, peels	Iridoid glucoside (ajugol) and two phenols *p*-hydroxybenzoic acid, methyl *p*-hydroxybenzoate	Iridoid glycoside, phenols	*Cladosporium herbarum*	Pianara et al. (2007)
60	*Taxus baccata* L., Taxaceae	Needles	Bilobetin	Flavones	*A. alternata*, *Cladosporium oxysporum*, *F. culmorum*	Krauze-Baranowska (2003)
61	*Thonningia sanguinea* Vahl., Balanophoraceae		Extracts	Saponins, quinines, polyphenols	*A. fumigatus*, *A. flavus*, *C. albicans*	Carpano et al. (2003)
62	*Toona ciliata* M. Roem., Meliaceae	Leaves	Toonaciliatin	Pimaradiene-type diterpenoid	*T. rubrum*	Chen et al. (2009)
63	*Toona ciliata* M. Roem., Meliaceae		Cedrelone, azadiradione, limonin, nomilinic acid	Tetranotri terpenoids	*Puccinia arachidis*	Govindachari et al. (2000)
64	*Tordylium apulum* L., Apiaceae	Aerial parts	Flavonoid diglycoside, a coumarin	Coumarin, Flavonoid	*Cladosporium cucumerinum*	Kofinas et al. (1998)
65	*Vochysia divergens* Pohl, Vochysiaceae	–	Sericic acid		*C. albicans*, *C. tropicalis*, *Penicillium*	Hess, et al. (1995)
66	*Wedelia paludosa* DC., Asteraceae	Flower	Kaurenoic acid, luteolin	Flavone	*Epidermophyton floccosum*, *T. mentagrophytes*	Sartori et al. (2003)
67	*Zuccagnia punctata* Cav., Fabaceae	Fruits, aerial parts	(i) 2,4-Dihydroxy-3-methoxy chalcone (ii) 2,4-Dihydroxy chalcone	Chalcone	*M. gypsum*, *T. rubrum*, *T. mentagrophytes*	Svetaz et al. (2007)

Table 5.2 Antifungal compounds from essential oils of medicinal plants

Sl. no.	Botanical name	Compound	Effective against	Reference(s)
1	*Haplophyllum tuberculatum* (Forsskal) A. Juss	α- and β-Phellandrene, limonene, β-ocimene, β-caryophyllene and myrcene	*Curvularia lunata* and *Fusarium oxysporum*	Al-Burtamani et al. (2005)
2	*Thymbra capitata* (L.) Cav.	γ-Terpinene and p-cymene	*Candida*, *Aspergillus*, and dermatophyte	Salgueiro et al. (2004)
3	*Lavandula stoechas* L.	Fenchone, limonene, and myrtenol	*Rhizoctonia solani*	Angioni et al. (2006)
4	*Rosmarinus officinalis* L.	α-Pinene, borneol, camphene, camphor, verbenone, and bornyl acetate	*Candida albicans*	Dalleau et al. (2007)
5	*Lavandula angustifolia*	Linalool and linalyl acetate	*Candida albicans*	D'Auria et al. (2005)
6	*Mentha piperita* L.	Menthol	*Aspergillus flavus* and *A. parasiticus*	Farag et al. (1989)
7	*Thymus vulgaris*	Thymol	*Aspergillus flavus* and *A. parasiticus*	Farag et al. (1989)
8	*Salvia mirzayanii* Rech. F. and Esfand.	Linalool, linalyl acetate, α-terpinyl acetate, 1,8-cineole, α-cadinol, and δ-cadinene	*Fusarium solani* and *Candida albicans*	Portillo et al. (2005)
9	*Calocedrus formosana* Florin.	α-Cadinol and murolol	*Lenzites betulina*, *Pycnoporus coccineus*, *Trametes versicolor*, and *Laetiporus sulphureus*	Cavaleiro et al. (2006)
10	*Trachyspermum ammi* (L.) Sprague	Thymol, p-cymene, γ-terpinene, β-pinene, and terpinen-4-ol	*Aspergillus niger*, *Fusarium moniliforme*, and *Curvularia lunata*	Nigam and Rao (1977)
11	*Cuminum cyminum* L.	β-Pinene, γ-terpinene, and cuminaldehyde	*Aspergillus*	Patra et al. (2002); Kawther (2007); Hammer et al. (2002)
12	*Foeniculum vulgare* Mill.	Trans-anethole	*Alternaria alternata*, *Fusarium oxysporum*, *Aspergillus flavus*, and *A. parasiticus*	Aggarwal et al. (2000); Shabnam et al. (2012).
13	*Bupleurum gibraltaricum* Lamarck.	Sabinene, α-pinene, and 2,3,4-trimethylbenzaldehyde	*Plasmopara halstedii*	Komiya et al. (2006)
14	*Zingiber officinale* Roscoe	Zingiberene	*Aspergillus flavus*, *A. parasiticus*, and *F. oxysporum*	Pandey et al. (2010); Farag et al. (1989)
15	*Curcuma longa* L.	Terpinolene, α-phellendren, and terpinene-4-ol	Dermatophyte	Apisariyakul et al. (1995); Saha R and Bhupendar (2011)
16	*Nigella sativa* L.	Thymoquinone	*Candida albicans*, *Aspergillus flavus*	Mashhadian and Rakhshandeh (2005); Khan et al. (2003); Aggrawal et al. (1979); Amrouche et al. (2011); Singh et al. (2005); Al-Jabre et al. (2005); Zhang et al. (2006)
17	*Syzygium aromaticum* (L.) Merrill and Perry	Eugenol	*Candida*, *Aspergillus*, and dermatophyte	Eugenia et al. (2009)

(continued)

Table 5.2 (continued)

Sl. no.	Botanical name	Compound	Effective against	Reference(s)
18	*Lavandula angustifolia* Mill.	Linalool and linalyl acetate	*Candida albicans*	D'Auria et al. (2005)
19	*Rosmarinus officinalis* L.	α-Pinene, borneol, camphene, camphor, verbenone, and bornyl acetate	*Fusarium graminearum*	Angioni et al. (2004)
20	*Tagetes patula* L.	Piperitone and piperitenone	*Botrytis cinerea* and *Penicillium digitatum*	Romagnoli et al. (2005)
21	*Calocedrus formosana*	α-Cadinol and murolol	*Lenzites betulina*, *Pycnoporus coccineus*, *Trametes versicolor*, and *Laetiporus sulphureus*	Cheng et al. (2004)
22	*Trachyspermum ammi* (L.) Sprague	Thymol, *p*-cymene, γ-terpinene, β-pinene, and terpinen-4-ol	*Aspergillus niger*, *Fusarium moniliforme*, and *Curvularia lunata*	Singh et al. (2004)

5.1.9 Future Prospectus of Plant-Derived Antifungal Drug

Fungal pathogens, namely, the species of *Trichophyton*, *Microsporum*, *Epidermophyton*, *Aspergillus*, *Candida*, etc., have become prevalent in causing diseases in human beings and animals. The increase in fungal infections in human beings and emergence of resistance in pathogens are serious problems in the healthcare system. The unscientific way of using antifungal drugs for prophylactic or therapeutic purposes or for agricultural purposes has provided selective pressure on the survival and spread of resistant organisms. To overcome this emerging global problem, the policy makers, pharmaceutical industries and funding agencies have to create a platform for the scientists to develop new strategies and new antifungal drugs for the management of fungal diseases. As plants have proved to have very strong properties of inhibiting fungal growth without any residual side effect on the human body, the traditionally used medicinal plants could be the best source for the development of new antifungal drugs.

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