Review Article

A Review to Search Novel Antifungal Principles from Bioactive Plants: The Hidden Treasure

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Abstract

Now–a-days, fungal infections of the skin are very common in Bangladesh as like as the other countries in the world. Surprisingly, these infections have become very difficult to treat and cure permanently. We know that, skin takes part in many vital functions of the body as it is the largest organ. It maintains the temperature & salt-water balance and protects the internal organs from the external noxious environment. It is also involved in synthesis and excretion of many vital constituents of the body. Damage to the skin by various noxious stimuli like burns, injuries or infections are major concerns in Dermatology. At present, most of the health care providers in Bangladesh are facing serious problems due to the emergence of resistance to available anti-fungal drugs. The nature is considered as the hidden treasure of medicines. Innumerable natural compounds are used worldwide due to their acceptable margin of efficacy, safety & cost. The present review is involved to find out 24 (twenty four) bioactive plants used in rural Bangladesh as folklore medicines to treat various skin diseases including the fungal ones. Further researches are recommended immediately to identify, separate and assess the antifungal efficacy of bioactive principles present in these plants. Successful screening of the resistant fungal strains and their interaction with these bioactive compounds would also be an interesting era of study. Hopefully, the most promising compounds would be developed as newer medicines and manufactured commercially to combat the increasing burden of fungal epidemics.

Key words: *Antifungal Principles, Bioactive Plants*

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Justification of the study

The alarming rate of increase in fungal infections and the emerging resistance to antifungal drugs have created the necessity to discover newer & effective antifungal drugs. The fungal diseases have become widespread as epidemics and people are suffering chronically despite of modern treatment approaches. The ongoing pandemics of diabetes, stroke, cancer and use of immunosuppressive agents have made the patients prone to develop fungal infections quite inevitably. Under these circumstances, review and researches directed in search of novel anti-fungal agents is a craving need for medical science. Different plants with numerous bioactive principles could be considered as the hidden treasure in this field of research.

Introduction

Fungal infection of the skin

The largest organ of the body, the skin. has many functions, including protection from external noxious environment, temperature regulation, water balance, synthesis of chemical compounds etc.[1] Fungal infection, also known as mycosis, is becoming serious health problem in the world specially Bangladesh.[2-4] It can cause infection, affect both human and animal. In human, this infection occur in any part of the body. Fungi can live in the air, soil, water, and plants. There are also some fungi that live naturally in the human body.[2-4] Like many microbes, there are helpful fungi and harmful fungi. When harmful fungi invade the body, they can be difficult to kill, as they can survive in the environment and re-infect the person trying to get better.[2-4]

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It was estimated that about 20%-25% of the world's population has some form of fungal infection. Among them oral candidiasis, Tineasis, Pityriasis versicolor, Onychomycosis are common fungal infections in our country.[5]

Most mycotic infections are superficial and are limited to the stratum corneum, hair and nails.[5] (Figure 1.1 & Figure 1.2). Deep mycosis are sometimes life threatening. They are found more common in immunosuppressive patients, including AIDS, transplant recipients those on corticosteroid or immunosuppressive agents therapy. Actinomycosis, sporotridrosis and blastomycosis are some examples of deep fungal infections in human.[6] (Figure 1.3)

Figure 1.1: Superficial mycosis.

Most mycotic infections are superficial and limited to the stratum cornium, hair and nails. The Figure 1.1 shows a patient is suffering from superficial mycosis affected in the skin of the chest. Source.: https://www.microbiologybook.org/mycology/2018mycology-4.htm

Figure 1.2: Superficial mycosis for example Tinia capitis

affecting his scalp. Source.: https://depositphotos.com/stock-photos/tinea-capitis.html

Figure 1.3: Deep mycosis for example coccidioidomycosis

The Figure 1.3, shows a patient is suffering from deep mycosis affecting in the skin of the thigh and leg. Source: Photograph ref: https://www.msdmanuals.com/professional/infectious-diseases/fungi/coccidioidomycosis Current treatment.[11,12]

Table 1.1: Antifungal drugs currently used in superficial and deep mycosis.

S. No	Class	Drugs	Uses
1.	Azole antifungals	Clotrimazole, Econazole, Isoconazole, Miconazole, Ketoconazole, Itraconazole	Topical fungal infections, Candidiasis, aspergillus and candida infections, vaginal yeast infections
2.	Echinocandins	Caspofungin, Micafungin	Esophageal Candidiasis, Salvage therapy
4.	Polyenes	Amphotericin B, Nystatin	Systemic mycosis, superficial mycosis
5.	Phenolic cyclohexane	Griseofulvin	Dermatophytic infections
6.	Synthetic pyrimidines	Flucytosine	Cryptococcosis, severe invasive aspergillosis, cryptococcal meningitis treated along with other antifungals
7.	Morpholines	Amorolfine	Topical fungal infections
8.	Pyridines	Buthiobate, Pyrifenox	Dermatophytic infections, Tinea conditions
9.	Phthalimides	Captan	Invasive dermatophytic conditions and candida infections

The emergence of resistance against most of the antifungal drugs

Many researchers revealed the alarming situation that most of the clinically proven previous antifungal drugs are going to resistant against pathogenic fungus. They have also mentioned that the high burden and growing prevalence of invasive fungal infections (IFIs), the toxicity and interactions associated with current antifungal drugs, as well as the increasing resistance, ask for the development of new antifungal drugs, preferably with a novel mode of action. There is an increased awareness of the morbidity and mortality associated with fungal infections caused by resistant fungi in various groups of patients. Epidemiological studies have identified risk factors associated with antifungal drug resistance.[7-9]

Some scientists have notified that, though the improvement of antifungal therapies occurred over 30 years, the phenomenon of antifungal resistance is still of major concern in the clinical practice. In this connection they gave emphasis in the identification of new antifungal which is achieved by the screening of natural or synthetic chemical compound collections.[10]

The epidemiological data suggest that the incidence and prevalence of serious mycoses continues to be a public health problem. The increased use of antifungal agents has resulted in the development of resistance to these drugs. The spread of multidrug-resistant strains of fungus and the reduced number of drugs available make it necessary to discover new classes of antifungals from natural products including medicinal plants.[10] Many compounds that have anti-fungal properties are derived from medicinal plants. These products , either as pure single compound or as purified extracts, provide promising opportunities for new anti-fungal principles development. The main goal of these study is to selection, compilation and further investigation of promising bioactive plants against resistance strains of fungus.[10]

Antifungal drugs that are derived from plants currently used or proposed to be used in the treatment of various fungal infections are listed below:

Table 1.2: List of plants having antifungal activity against pathogenic fungi .[13-22,17-26]

Sl. no.	Botanical name	Family	Parts used	Chemical class	Microorganism tested
1.	Eugenia uniflora	Myrtaceae	Leaves	Sesquiterpenes, Monoterpene, hydrocarbons	C. albicans, C. dubliniensis, C. glabrata, C. krusei [13]
2.	Psidium guajava	Myrtaceae	Leaves	Methanolic extract	C. albicans, C. dubliniensis, C. glabrata, C. krusei [13]
3.	Curcuma longa	Zingiberaceae	Rhizome	Turmeric oil	C. albicans, C. dubliniensis, C. glabrata, C. krusei [13]
4.	Piptadenia colubrina	Mimosaceae	Stem bark	—	C. albicans, C. dubliniensis, C. glabrata [13]
5.	Schinus terebinthifolius	Anacardiaceae	Stem bark	Extract	C. albicans, C. dubliniensis [13]
6.	Persea americana	Lauraceae	Leaves	Chromene	C. albicans C. dubliniensis C. glabrata, C. krusei [13]
7.	Parapiptadenia rigida	Fabaceae	Stem bark	Pyrrolidine amide	C. albicans [13]
8.	Ajania fruticulosa	Asteraceae	Fruits	Guaianolides	Candida albicans, C. glabrata A. fumigatus [13]
9.	Alibertia macrophylla	Rubiaceae	Leaves	Extract	Cladosporium sphaerospermum; C. cladosporioides; A. niger; Colletotrichum gloeosporioides [13]
10.	Aniba panurensis	Lauraceae	Whole plant	—	C. albicans [13]
11.	Aquilegia vulgaris	Ranunculaceae	Leaves and stems	Bis (benzyl)	A. niger [13]

Sl. no.	Botanical name	Family	Parts used	Chemical class	Microorganism tested
12.	*P. regnellii*	Piperaceae	Leaves	Extract	*Trichophyton rubrum, Trichophyton mentagrophytes, Microsporum canis* [14]
13.	*Rubia tinctorum*	Rubiaceae	Root	Triterpene	*A. niger, Alternaria alternaria, P. verrucosum, Mucor mucedo* [15]
14.	*Tithonia diversifolia*	Asteraceae	Whole plant	Contained saponins, Polyphenols	*Microbotryum violaceum, Chlorella fusca* [16]
15.	*Vernonanthura tweedieana*	Asteraceae	Root	Extracts	*T. mentagrophytes* [17]
16.	*Zingiber officinale*	Zingiberaceae	Rhizomes	Steroidal saponin	*P. oryzae* [18]
17.	*Datura metel*	Solanaceae	Whole plant	Diterpenoid, Alkaloids	*C. albicans, C. tropicalis* [19]
18.	*Lupinus albus*	Leguminosae	Leaf surface	—	*T. mentagrophytes* [20]
19.	*Ecballium elaterium*	Cucurbitaceae	Fruit	Extract	*Boitylis cinerea* [21]
20.	*Cassia tora*	Leguminosae	Seeds	Anthraquinone	*Candida albicans* [22]
21.	*Chamaecyparis pisifera*	Cupressaceae	Leaves and Twigs	Isoflavone	*P. oryzae* [23]
22.	*Prunus yedoensis*	Rosaceae	Leaves	Diterpenes	*C. herbarum* [24]

Table 1.3: List of plants having antifungal activity against plant pathogenic fungi[25-26]

Sl. no.	Botanical name	Family	Parts used	Chemical classes	Microorganism tested
1	Citrus reticulata	Rutaceae	Peels	99% of the oil contained limonene , geranial, neral, geranyl acetate, geraniol, b - caryophyllene, nerol, neryl acetate.	Alternaria alternata (Aa), Rhizoctonia solani (Rs), Curvularia lunata (Cl), Fusarium oxysporum (Fo) and Helminthosporium oryzae (Ho)
2	Heliotropium indicum	Boraginaceae	A erial parts	Pyrro lizidine alkaloids, flavonoids, and terpenoids.	Trichoderma longibrachiantum, Aspergillus flavus, Aspergillus niger, Fusarium solani and Candida albican

Conclusion and recommendation

Health care providers are facing troubles in treating fungal infections because of reduced effectiveness and increased resistance to antifungal drugs. So, searching of newer compounds from plant sources should be reinforced. The plants mentioned in this article could serve as a list of potential candidates for further research on antifungal agents.

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