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Review Article

ANTIDERMATOPHYTIC ACTIVITY OF ANGIOSPERMIC PLANTS: A REVIEW

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ABSTRACT

In recent years, there has been increasing interest worldwide in the use of alternative/herbal medicine for the prevention and treatment of fungal diseases. Currently, however, quality-related problems (lack of consistency, safety, and efficacy) seem to be overshadowing the potential genuine benefits of various herbal products for the treatment of fungal diseases. Extracts obtained from many plants have recently gained a great popularity and scientific interest. Since the middle ages, natural plant preparations have been widely used for treatment of fungal diseases. Treatment of the fungal pathogen is becoming increasingly difficult due to antifungal drug resistance, especially with fluconazole, which is a commonly used azole. This paper reviews the *in vitro* activity of angiospermic plant extracts and their major compounds against dermatophytes and also a compilation of updated information on angiospermic plant extracts with antifungal properties.

Keywords: Dermatophytes, Extracts, Medicinal plants.

INTRODUCTION

Dermatophytosis poses a serious problem to the socio-economically backward population. Superficial infections caused by keratinophilic fungi are called ringworm infections or tinea infection. The disease is predominant in tropical to subtropical regions of the world due to their prevailing moisture and temperature conditions, which further aggravate the problem [1,2]. The incidence of dermatophytic infections has increased considerably during the past decade [3]. Dermatophytoses, considered as zoonosis, have created more public health concerns due to close contact between humans - particularly children - and animals such as dogs, cats, birds, and small rodents or pocket pets. The clinical symptoms may not pose a serious threat, but effective treatment is usually costly and time-consuming.

Although a large number of synthetic allopathic drugs are available in the market. The majority of these clinically used antifungals suffer from various drawbacks in terms of toxicity, lack of fungal efficacy cost and emergence resistant strains caused by the frequent use of them. In recent years, there has been an increasing search for new antifungal compounds due to the lack of efficacy, side-effects and or resistance associated with some of the existing drugs [4,5]. A large number of plants/plant extracts/decoctions or pastes are being used since ages as home remedies by layman and traditional medicinal practitioners in India for treatment of fungal diseases. Several methodologies used by various researcher to extract antifungals from plants. The present review work was designed to evaluate the potential of various preparations and plant extracts against dermatophytes causing infection in the skin, hair and nail, etc.

ANTIDERMATOPHYTIC ACTIVITY OF ANGIOSPERMIC PLANTS

In vitro investigation of some medicinal plant species and their preparation have been published confirming the effect of whole plant parts, preparations, oils and their major compounds on dermatophytes causing various types of skin, nail, and hair infection are summarized below in the text and Table 1.

Due to increasing resistance to antifungal compounds and reduced number of antifungal drugs lead us to search new alternatives among medicinal plants, their preparations, essential creams and oils used for anti-dermatophytic activity.

Essential oil of *Eucalyptus rostrata* leaves was tested against four dermatophytes, namely, *Trichophyton mentagrophytes, Epidermophyton floccosum, Microsporum gypseum* and *Microsporum canis* [6].

Anti-dermatophytic activity of aqueous and ethanolic extracts of neem leaves were tested against 88 clinical isolates of dermatophytes. Ethanolic extract was found to possess more activity as campared to aqueous extract [1].

Essential oils of 14 plant species were tested against dermatophytes, namely, *E. floccosum* and *M. gypseum* also showed broad anti-dermatophytic spectrum when tested against *Aspergillus flavus, Asperigillus niger, E. floccosum, Microsporum audouinii, M. gypseum, Microsporum nanum, Trichophyton rubrum* and *Tricholosporum violaceum* [7].

Antifungal activity of *Catharanthus roseus* leaves was tested at 5% and 10% concentrations against dermatophytes and related keratinophilic fungi, as *M. gypseum, Trichophyton simii* and *Malbranchea gypsea* or *Chrysosporium tropicum* and *Candida tropicum* [8].

Medicinal plants of Chhindwara district of Madhya Pradesh were tested for anti-dermatophytic activity against *T. mentagrophytes*, a causal agent of tinea pedis. Leaves and stems extracts of *C. roseus* showed good activity against *T. mentagrophytes*. Stem of *C. roseus* showed highest antifungal activity (77.7%) of water extract, whereas water extract of leaves reported 40.1% antifungal activity [9].

Some new antifungals agents including clotrimazole, miconazole, fluconazole (FLC), itraconazole and ketoconazole (imidazole group) were also effective but they can cause side effects, which could be harmful to human health [10].

Essential oils of six *Cymbopogon citrates* were tested against dermatophytes, namely, *M. gypseum, Microsporum* sp., *T. rubrum* and *E. floccosum.* The essential oil of *Lantana camara* showed higher activity against all dermatophytes as compared to other test oils [11].

Medicinal plants from South India were tested for anti-dermatophytic activity against four isolated species of *T. mentagrophytes*. Ethanol extract was found to be effective than water extract against *T. rubrum* and *T. mentagrophyte* [12].

Table 1: Anti-dermatophytic activities of some plant extracts

S. no.	Plant species	Parts/ preparations used	Methods used	Solvents used	Dermatophytic species tested	Results	References
1.	Medicinal plants of Chhindwara district	Leaves and stem	-	-	*T. mentagrophytes*	Stem of *C. roseus* showed highest antifungal activity (77.72%) of water extract	[9]
2.	Six plant	Oils	-	-	*M. gypseum, Microsporum* sp., *T. rubrum* and *E. floccosum*	The essential oil of *L. camara* showed higher activity against all dermatophytes as compared to other test oils	[11]
3.	Medicinal plants from South India	-	-	Ethanol	*T. rubrum and T. mentagrophytes*	Ethanol extracts of plants exhibited more activity than water extracts	[12]
4.	*P. stratiotes*	Leaf	Well diffusion	Methanol	*T. mentagrophytes, T. rubrum, M. gypseum and M. nannum, E. floccosum*	Methonolic extract was found to be most active against dermatophytes *T. rubrum, T. mentagrophytes* and *E. floccosum* at 250 ml	[13]
5.	Ozanized olive	Oil	Agar dilution	-	*A. fumigatus, C. albicans, E. floccosum, M. canis and T. rubrum*	Among all the species mentioned above, *M. canis* and *T. rubrum* showed maximum susceptibility	[15]
6.	*P. betle*	Cream	Disc diffusion	Ethanol	*M. canis, M. gypseum, and T. mentagrophyte*	The results suggested a promising antifungal property of *P. betle* extract	[14]
7.	*C. fistula*	Flowers extracts	Disc diffusion	Hexane, chloroform, ethyl acetate, methanol and water	*T. mentagrophytes* and *E. floccosum*	Ethyl acetate extract alone showed highest activity against six fungal organisms	[42]
8.	*C. obvata Collad*	Leaves and shoot	-	Ethanol, methano, ethylacetate, chloroform and aqueous extracts	*M. gypseum, T. tonsurance* and *T. rubrum, A. niger, A. flavus*	The aqueous extract showed maximum inhibition activity against test dermatophytes, as compared	[16]
9.	*C. alata* linn	Flower	Liquid dilution	Methanol	*M. audounni, A. flavus, A. parasiticus*	Aqueous flower extract of *C. alata* showed potential antifungal agent against these three fungi	[43]
10.	*G. javanica* Miq.	Leaves	Disk diffusion	-	*T. mentagrophytes, A. niger*	Showed strong (+++) antifungal activity against *A. niger* (++) against *C. albicans* (+) against *T. mentagrophytes*	[44]
11.	*C. citrates* DC., *L. camara* L., *N. oleander* L., *O. basilicum* L., *O. europaea* L.,	Stalk, leaves, flower and stem	Well diffusion	Ethyl alcohol, methanol, n-butanol, ethyl-acetate or chloroform	*T. mentagrophytes, T. verrucosum, M. gypseum* and *M. canis, E. floccosum*	The methanol extract of lemon grass, *lanta* and *nerium* followed by their ethyl acetate extracts showed the highest activities against *T. rubrum*	[18]
12.	*S. dulcamara* L.	Roots Stems Leaves Flowers Berries	Filter paper disc	-	*M. gypseum, T. rubrum, mentagrophytes*	Best activity was found against *M. gypseum* with inhibition zone of *T. mentagrophytes* was found to be larger than ketoconazole	[20]
13.	*E. camaldulensis*		In vitro tube dilution	Ethanol	*M. canis, M. gypseum, T. rubrum* and *verrucosum*	Water in oil formulation showed maximum inhibitory effect	[17]
14.	*D. quercifolia* (L.)	Dried rhizome	Agar dilution and disk diffusion	Ethanol, methanol, acetone, di-athyl ether and water	*T. mentagrophytes, M. canis, M. gypseum, T. rubrum* and *E. floccosum*	The ethanol extracts was found to be possess anti-dermatophytic activity with clear zone due to presence of triterpenes and coumarins	[19]
15.	*P. parviflorus*	Leaf	Agar dilution method	Ethanol	*M. canis, M. gypseum, E. floccosunm, T. rubrum, T. mentagrophytesc*	Ethyl acetate extract was shown in the form of triterpenes responsible for anti-dermatophytic activity of this plant	[45]

(*Contd*...)

Table 1: (*Continued*)

S. no.	Plant species	Parts/ preparations used	Methods used	Solvents used	Dermatophytic species tested	Results	References
16.	*A. sativum*, *C. martinii* and *C. roseus*	Leaves, stems, flowers, roots	Disc diffusion	-	*T. rubrum*, *T. mentagrophytes* and *M. gypseum*	Free flavonoid and bound flavonoid extracts showed maximum inhibitory effect against pathogenic fungal species	[22]
17.	Epigallocatechin 3-0 gallate	Isolated compound	-	-	*35 dermatophytes*	Secondary metabolites showed maximum inhibitory effect against the clinical isolates of dermatophytes	[23]
18.	*P. longum*	Root	-	Methanol	*Three genera of keratinophillic fungi*	Methonolic extract showed inhibition zone between 3 mm and 11 mm against all the isolated species of keratinophilic fungi	[24]
19.	*Curcuma viz., C. angustifolia, C. aromatica, C. domestica and C. zedoaria*	Oil	-	-	*E. floccosum, M. gypseum and T. rubrum*	Extract of *C. domestica* showed maximum inhibitory effect on various fungal species at different concentration	[21]
20.	*M. piperata*	Oil	-	Methanol, ethanol, ethylacetate	*M. canis* and *T. rubrum*	Ethanolic extract of leaves of *M. piperita* exhibited the strongest activity against *T. rubrum, M. canis*	[29]
21.	Clotrimazole and cinnamon	Oil	Broth microdilution	-	*M. canis, T. rubrum, T. verrucosum, mentagrophytes E. floccosum*	Terbinafine was found to be the most effective anti-mycotic agent	[47]
22.	*Calotropis*	Leaves	-	-	*T. rubrum, T. tonsurans, T. mentagrophytes, E. floccosum* and *A. flavus*	Chloroform extract showed maximum activity against pathogenic fungi as compared to methanol and ethyl acetate leaf extract	[27]
23.	*A. lebbeck, A. reticulata, C. fistula, C. guianensis, W. tinktoria*	Bark and leaf	Agar-well diffusion	Hexane, methanol, ethyl acetate	*T. rubrum*	*A. reticulata* leaf and bark extracts showed maximum activity against *T. rubrum* than other plants	[28]
24.	*R. scelaratusa, P. pinnata*	Whole plant extract	Agar-well diffusion	Chloroform methanol and water	*T. tonsurans, T. mentagrophytes, T. rubrum, M. gypseum* and *M. fulvum*	The minimum inhibitory concentrations of the extracts were determined by broth macro dilution method	[26]
25.	*Datura, Datura* *Dube* *Lantana* Neem Neem	Leaf, Seed Grass Leaf Leaf Seed	Food poising	Plant water extracts	*T. rubrum and C. albicans*	Neem and *Datura* water extracts showed their maximum effect against *T. rubrum* and *C. albicans* respectively	[25]
26.	*C. langsdorffii*	Leaf	-	Ethanol	*M. canis, M. gypseum, T. rubrum, T. mentagrophytes*	The results stimulate the achievement of *in vivo* assays to confirm the benefits of the application of oleoresin extracted from copaiba in the treatment of dermatophytosis	[49]
27.	*C. procera*	Hydroalcoholic extracts	Dilution agar	Ethanol	*T. mentagrophytes, T. rubrum, M. canis, E. floccosum*	The ethanolic extract of *C. procera* leaves was found to inhibit all the species of dermatophytes	[31]

T. mentagrophytes: Trichophyton mentagrophytes, C. roseus: Catharanthus roseus, M. gypseum: Microsporum gypseum, E. floccosum: Epidermophyton floccosum, T. rubrum: Trichophyton rubrum, L. camara: Lantana camara, P. stratiotes: Pista stratiotes, M. nannum: Microsporum nannum, A. fumigatus: Aspergillus fumigatus, C. albicans: Candida albicans, M. canis: Microsporum canis, P. betle: Piper betle, C. fistula: Cassia fistula, C. obvata: Cassia obvata, T. tonsurance: Tricophyton tonsurance, A. niger: Aspergillus niger, A. flavus: Aspergillus flavus, C. alata: Cassia alata, M. audounni: Microsporum audounni, G. javanica: Gouania javanica, C. citrates: Cymbopogon citrates, N. oleander: Nerium oleander, O. basilicum: Ocimum basilicum, O. europaea: Olea europaea, T. verrucosum: Trichophyton verrucosum, S. dulcamara: Solanum dulcamara, Eucalyptus camaldulensis: Eucalyptus camaldulensis, D. quercifolia: Drynaria quercifolia, P. parviflorus: Pogostemon parviflorus, E. floccosunm: Epidermophyton floccosunm, A. sativum: Allium sativum, C. martinii: Cymbopon martinii, P. longum: Piper longum, C. angustifolia: Curcuma angustifolia, C. aromatica: Curcuma aromatica, C. domestica: Curcuma domestica, M. piperata: Mentha piperata, A. lebbeck: Albizia lebbeck, A. reticulata: Annona reticulata, C. guianensis: Couroupita guianensis, W. tinktoria: Wrightia tinktoria, R. scelaratusa: Ranunculus scelaratusa, P. pinnata: Pongmia pinnata, Trichophyton tonsurans, M. fulvum: Microsporum fulvum, C. langsdorffii: Copaifera langsdorffii, C. procera: Calotropis procera

Anti-dermatophytic activity of methonolic leaf extract of *Pistia scleratus* was tested against *T. rubrum*, *T. mentagrophytes, M. gypseum, M. nanum, E. floccosum*. Methonolic extract was found to be most active against dermatophytes *T. rubrum, T. mentagrophytes* and *E. floccosum* at 250 mg/ml while against *M. gypsum and M. nanum,* the values were 125 mg/ml [13].

Alpinia galanga rhizomes, piper betle leaves (piperaceae*) Allium ascalonicum* bulbs (Liliaceae) extracts were tested against *M. canis, M. gypsum and T. mentagrophyte.* Out of which piper betle extract showed promising antifungal activity. Formulation of 10% piper betle cream was tested against zonotic dermatophytes [14].

Various pathogenic fungi *(Aspergillus fumigatus, Candida albicans, E. floccosum, M. canis* and *T. rubrum* were tested for effectiveness of ozanized olive oil (oleozone) by using agar dilution method. Among all the species mentioned above, *M. canis* and *T. rubrum* showed maximum susceptibility. While *M. canis* did not show any inhibition zone [15].

Extract of 14 herbs were tested against isolated fungal species namely *Microsporum*, out of which garlic was found to most effective against *Microsporum* and other species. Apart from these herbals while lutsi, voriander, methi, heena, and green onion did not show any effect on isolated fungal species by hair bating technique. Leaves of *Cassia obvata* colland were extracted with different solvents and tested against pathogenic fungus *A. flavus, A. niger, M. gypsum, Trichopyton tonsourons and T. rubrum.* As compared to other solvent aqueous extract showed maximum inhibitory effect against the dermatophytes [16].

Hydro-alcoholic extract of *Eucalyptus camaldulensis* was tested against dermatophytes by using *in vitro* dilution technique. Finally, a formulation was prepared which showed maximum water oil inhibitory effects against dermatophytes. Water in formulation showed maximum inhibitory effect [17].

In vitro antifungal activity was investigated by using different organic solvent of some medicinal plants against *M. canis, M. gypseum, T. mentagrophytes, Trichophyton verrucosum* and *E. floccosum.* Maximum activity was shown by lemon extract. While nerium and basil showed moderate activity instead, olive extract showed the least activity against pathogenic fungal species [18].

Drynaria quercifolia used by tribals in Maharashtra was tested for anti-dermatophytic activity against *T. mentagrophytes, M. canis, M. gypseum, T. rubrum* and *E. floccosum* by using agar dilution and disk diffusion method. The ethanol extracts isolated by thin layer chromatography was found to possess anti-dermatophytic activity with clear zone due to the presence of triterpenes and coumarins (antifungal compounds) [19].

Identified alkaloid from roots extract of *Solanum dulcamara* was found to possess anti-dermatophytic activity against *T. rubrum, T. mentagrophytes, M. gypseum.* Best activity of root extract was found against *M. gypseum* with inhibition zone of *T. mentagrophytes* was found to be larger than ketoconazole [20].

Evaluation of essential of *Curcuma* species was screened for anti-dermatophytic activity of *T. rubrum* and *M. canis* by broth dilution method. Extract of *Curcuma domestica* showed maximum inhibitory effect on various fungal species at different concentration. These extracts did not show any activity below 5°C on dermatophytes [21].

Plants of *Allium sativum, Cymbopogen martinii* and *C. roseus* were screened for their anti-mycotic activity by using disc diffusion method. Water extract methanol, free flavonoids and bound flavonoids of various plants were tested against *T. rubrum, T. mentagrophytes* and *M. gypseum.* Free flavonoid and bound flavonoid extracts showed maximum inhibitory effect against pathogenic fungal species [22].

Based upon previous reports of epigallocatechin 3-0 gallate inhibitory effects on chemical isolated, the same work was repeated and tested against 35 dermatophytes. Their isolates showed maximum susceptibility than those of other antifungals. Activity of (EGCg) was found 4 times higher than FLC and 16 times higher than flucytosine. Secondary metabolites showed maximum inhibitory effect against the clinical isolates of dermatophytes [23].

Methanolic root extract of *Piper longum* was evaluated against isolated species belonging to three genera of keratinophillic fungi, methonolic extract showed inhibition zone between 3 mm and 11 mm against all the isolated species of keratinophilic fungi while extract did not show any inhibitory effect on *Chrysosporum keratinophilium* [24].

Different parts of plants were tested for antifungal activity from Jaipur district Rajasthan by food poisoning technique. Maximum antifungal activity was showed by seeds and leaves of *Azadirachita indica* and *Datura* seed against *T. rubrum* [25].

Antifungal activity of *Ramunculeus sceleratus* and *Pongamia pinnata* was tested *in vitro* method. The extracts are chloroform, methanol and water extracts of the plants are evaluated for anti-ringworm activity of five strains *T. rubrum, T. mentagophytes, T. tonsourons, M. gypseum* and *Microsporum fulvum*. The method used to determine the inhibition zone of different extracts is Agar well diffusion. However, the minimum inhibitory concentrations of the extracts are determined by broth macro dilution method [26].

Leaves of *Calotropis* spp. were evaluated against *T. rubrum, T. tonsurans, T. mentagrophytes, E. floccosum* and *A. flavus* with different solvent by using agar well diffusion method. All the three samples showed anti-mycosis activity but chloroform extract showed maximum activity against pathogenic fungi as compared to methanol and ethyl acetate leaf extract [27].

Plant species of *Albizia lebbeck* and *Annona reticulata* were tested against *T. rubrum* in hexane, ethyl acetate, methanol. *A. lebbek* bark, *A. reticulata* leaf and bark extracts showed maximum activity against *T. rubrum* than other plants [28].

Mentha piperita leaves were tested *in vitro* against two species of dermatophytes i.e., *Tricophyton* and *M. canis*. Ethanolic extract of leaves of *M. piperita* exhibited the strongest activity against *T. rubrum, M. canis* [29].

Leaf extract of *Cassia ocidentalis*, *Cassia tora*, *Lawsonia intermis*, *Xanthium inermis* and *Caselpinaa bonducella*, with different solvents were tested against *Trichophyton tonsourns, metanogyphytes, rubrum, M. gypsum, E. floccosum.* Among other solvent ethylacetate was found to be best solvent, which showed maximum inhibitory effect against dermatophytes [30].

Calotrpes plocera leaves extracts were tested against three different genera of dermatophytes *viz*., *Microsporum, Trichophyton, and Epidermatophyton* by dilution agar method. The ethonolic extract of *Calotropis procera* leaves was found to inhibit all the species of dermatophytes [31].

Antifungal potential of plants belonging to eight families and their oils was reviewed. They suggested that essential oils are the potential source of antimicrobials of natural origin. Essential oils and extracts obtained from many plants have recently gained a great popularity and scientific interest. The plant oil has been reported to have antibacterial, antifungal, antiviral, anti-parasitic and anti-dermatophytic properties. Their literature survey presents a compilation of updated information on plant essential oils with antifungal properties [32].

In vitro antifungal activity of different synthetic, herbal shampoos and natural products were tested against clinical isolated species like *Malassezia, Trichophyton* and *Asperigillus* spp. Synthetic shampoos showed excellent inhibitory activity against *Trichophyton, Malassezia* spp. *A. flavus* and *A. niger* [33].

Antifungal activities of some plants have been reported by various researchers throughout the world like [34-41,46,48,50].

CONCLUSION

Review of literature indicates that angiospermic plants showed varied activity against fungal species namely *Trichophyton, Microsporum, Epidermatophyton* and other *Candida spp*. Literature indicates that much work has been done on the screening of various plants extracts, herbs and other compounds but no work has been done on further purification of anti-mycotic compound, flavonoids and bound flavonoids. All the plant species tabulated above showed different anti-mycosis activity. This suggest that certain phyto-chemicals isolated from plant spp. exhibit their antifungal potential only with phyto-constituents used in the form of preparations, oils, creams and decoctions. All the plants reviewed in this text were common in India and abroad and these species should be explored as potent herbal chemotherapeutic for dermatophytosis.

Review summarized above confirms potential uses of extracts for anti-dermatophytic activity. Use of plant extracts in the treatment regimen of various diseases is gaining importance as antifungal properties of plant were now recognized by several workers. Each type of extract was also well defined by the way it is prepared and nature of the solvent used for the extraction process. In each of the extraction process plant material, creams and preparations were extracted in polar and less polar solvents and tested against fungi causing the skin infection.

In view of the anti-mycotic potentiality of plant, preparations and oils recommended for isolation, identification, characterization of isolated compound and toxicity studies on the antifungal principles and their fractions, preparations, creams for establishing cheaper, affordable and acceptable herbal products for further use. Review summarized above is very much helpful in curing dermatophytic infection as an application from biotechnological point of view. Reviews on *in vitro* testing were also helpful to determine the activities of new drugs and to find therapy. The ultimate conclusion of this study supports the traditional medicinal use of different plant extracts in treating different fungal infection.

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