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THERAPEUTIC PROPERTIES OF MEDICINAL PLANTS: A REVIEW OF PLANTS WITH ANTIFUNGAL ACTIVITY (PART 1)

Ali Esmail Al-Snafi*

Department of Pharmacology, College of Medicine, Thi qar University, Iraq.

ABSTRACT

Previous studies showed that medicinal plants exerted a wide range of antifungal activity. These plants included: *Adiantum capillus-veneris, Alhagi maurorum, Allium porrum, Allium sativum, Alpinia galangal, Ammi majus, Anchusa strigosa, Apium graveolens, Arachis hypogaea, Arundo donax, Asclepias curassavica, Asparagus officinalis, Avena sativa, Ballota nigra, Bellis perenni, Betula alba, Brassica rapa, Caesalpinia crista,Calamintha graveolens, Calendula officinalis, Calotropis procera, Capparis spinosa, Capsella bursa-pastoris, Capsicum annuum, Carum carvi, Cassia occidentalis, Chenopodium album* and *Chrozophora tinctoria*. This review was designed to highlight the antifungal effects of these medicinal plants.

Key words: Medicinal plants, Antifungal, Pharmacology, Therapeutics.

INTRODUCTION

Medicinal plants are the Nature's gift to human beings to help them pursue a disease-free healthy life, regarding treatment of the diseases and role in preserving health. Plants have been used as drugs by humans since thousands of years ago. As a result of accumulated experience from the past generations, today, all the world's cultures have an extensive knowledge of herbal medicine. Traditional medicine is based on beliefs and practices that existed before the development of so-called modern medicine or scientific drug therapy. However, the recent pharmacological studies showed that the medicinal plants exerted many pharmacological effects, among these the antifungal properties [1-35]. This paper was designed to highlight the antifungal effects of the medicinal plants.

Adiantum capillus-veneris

The water extracts and extracted phenols from gametophytes of *Adiantum capillus-veneris* showed antifungal activity against *Aspergillus niger* and *Rhizopus stolonifer* [36].

Alhagi maurorum

The antifungal effects of *Alhagi maurorum* was examined against *Aspergillus flavus, Alternaria alternate, Fusarium oxysporum, Fusarium solani, Bipolaris oryzae, Rhizoctnia solani, Pythium ultimum, Chetomium, Rhizopus and Mucor*. The result showed that the methanol extract of the plant exerted antifungal activity against some pathogenic fungi at 23 mg/ml concentration *Aspergillus flavus, Alternaria alternate, Fusarium oxysporum, Fusarium solani, Bipolaris oryzae, Chetomium* and *Mucor*, with a percentage of growth inhibition of 33.4, 89.4, 89.3, 94.6, 91.7, 59.0 and 94.1% [37].

Allium porrum

Spirostanol saponins isolated from *Allium porrum* showed antifungal activity [38].

Allium sativum

The effect of aqueous garlic extract on the macromolecular synthesis of *Candida albicans* was studied. Protein and nucleic acid syntheses were inhibited to the same extent as growth, but lipid synthesis was completely arrested. Blockage of lipid synthesis is likely an important component of the anticandidal activity of garlic [39]. A successful treatment of *Cryptococcal meningitis* was achieved by oral, muscular, and intravenous administration of garlic [40]. The antifungal activity in human serum against seven species of Candida and two species of Cryptococcus was detected after ingestion of garlic [41]. Garlic extract showed potent

*Corresponding Author **Ali Esmail Al-Snafi** E mail: aboahmad61@yahoo.com

antifungal activity against three different isolates of *Cryptococcus neoformans*. The minimum inhibitory concentration was 6 to 12 µg/mL. It also showed synergistic fungistatic activity with amphotericin B [41]. Pure allicin was also effective against *Candida*, *Cryptococcus*, *Trichophyton*, *Epidermophyton*, and *Microsporum* with MIC between 1.57 and 6.25 µg/mL. It inhibited germination of spores and growth of hyphae [42].

Alpinia galangal

It has been shown that essential oils from both fresh and dried rhizomes of galangal have antimicrobial activities against bacteria, fungi, yeast and parasite. Terpinen-4-ol, one of the monoterpenes in the essential oil from fresh galangal rhizomes, contains an antifungal activity against *Trichophyton mentagrophytes*. Acetoxychavicol acetate , a compound isolated from an n-pentane/diethyl ether-soluble extract of dried rhizomes, was active against some bacteria and many dermatophyte species [43-44]. *A. galanga* have antifungal activity against fungi resist the common antifungal products like amphotericin B and ketoconazole [45]. It exerted a concentration-dependent inhibition of the growth of zoonotic dermatophytes and the yeast-like *Candida albicans* [46]. Ethanolic extract of *A. galanga* posses phytotoxic activity against *Lemna minor* and significant antifungal activity against *Trichophyton longifusus* [47]. It also showed significant antifungal activity against *Candida albicans* and phytopathogenic fungi, *Colletotrichum musae* and *Fusarium oxysporum*, at a concentration of 10mg/ml [48]. 14 mg/ml of 1'-Acetoxychavicol acetate exerted antifungal activity against *Trichophyton mentagrophytes, Trichophyton rubrum, Trichophyton concentricum*, *Rhizopus stolonifer* and *Aspergillus niger* [44].

Ammi majus

Acetone and 95% ethanol extract of *Ammi majus* inhibited the growth of the *Neurospora crassa* fungi *in vitro* [49].

Anchusa strigosa

The aqueous extract of *Anchusa strigosa* (15 mg ml^{-1} medium) produced antifungal activity , the means of percentage of mycelial inhibition against M. canis *T. mentagrophytes* and *T. violaceum* were l50.1±9.84 , 36.7±3.80 , and 71.7±1.91 respectively [50].

Apium graveolens

The methanolic extract of all the examined celery showed positive antibacterial activity against all strains. Similarly, antifungal potential of the celery was determined against *Trichphyton longifuss, Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani and Candida glabrata* in concentration 200 µg/ml of dimethyl sulphoxide [51].

Arachis hypogaea

Peanut stilbenoids appear to play roles in plant defense mechanisms, they exerted antifungal effects when evaluated against economically important plant pathogenic fungi of the genera Colletotrichum, Botrytis, Fusarium, and Phomopsis [52, 54, 24 ,33].

Arundo donax

Arundo donax also exerted antifungal activity against four Basidiomycetes (*Trametes versicolor* CTB 863A , *Coniophora puteana* BAM Ebw.15, *Gloephyllum trabeum* BAM Ebw. 109, and *Postia placenta* FPRL 280) [55].

Asclepias curassavica

The crude extract of methanol was effective against *Clavibacter michiganense* than other extracts. The chloroform extract showed inhibition zone of 13mm, 19mm and 13mm against *Helminthosporium oryzae, Aspergillus niger* and *Fusarium oxysporum* respectively, whereas petroleum ether extract and methanol extract did not show any inhibition zone [56]. Ethanol and aceton extracts showed good anticandidal effect [57]. The latex sap terpens, cardenolids and glucanases also exerted antifungal activity. Fungi were deformed and emptied the cytoplasm. The sap exerted its effects on cell wall [58].

Asparagus officinalis

The saponin fraction of the *Asparagus officinalis* exerted antifungal activity [59-60].

Asphodelus fistulosus

Asphodelus fistulosus showed antifungal activity against *Trichophyton violaceum* [61].

Avena sativa

A protein fraction (P fraction) rich in Cys/Gly residues was extracted from oat (*Avena sativa*) seeds. Quantitative amino acid analysis and MS of the P fraction indicated that it contains a series of heterogeneous Cys/Gly-rich proteins with molecular masses of 3.6-4.0 kDa. Preliminary results showed that these proteins possessed weak to moderate antifungal properties to some fungal strains [62].

Ballota nigra

The essential oils from the aerial parts of *Ballota nigra* L. ssp foetida (Lamiaceae) collected at flowering and fruiting times, showed antifungal activity against nine plant pathogenic fungi [63]. Root and stem flavonoids, terpenes and phenols present in ethanol, chloroform, and ethyl acetate soluble fraction; these were found to be the most active inhibiting fractions against all the tested strains of bacteria, fungi, and leishmania. While in leaves flavonoids, terpenes, and phenols were present in ethanol, chloroform, and n-butanol fractions which were the most active fractions against both types of microbes and protozoan (leishmania) in in vitro study [64].

Bellis perenni

Bellis perenni extract showed *in vitro* and *in vivo* antifungal activity [39]. Triterpenoid glycosides obtained from *Bellis perennis* inhibited the growth of human-

pathogenic yeasts (Candida and Cryptococcus species). The intensity of growth inhibition is influenced particularly by the carbohydrate chains of the glycosides. Monodesmosidic as well as bisdesmosidic glycosides of polygalacic acid exert fungicidic effects [65].

Benincasa hispida

The antifungal activity of *Benincasa hispida* was studied against *Candida albicans* and *Aspergillus niger*. The methanolic extract of *Benincasa hispida* showed significant zone of inhibition against *Candida albicans* at the concentration of 30 mg/ml, while, it caused no inhibition against *Aspergillus Niger* [66].

Betula alba

Betulinic acid showed an inhibitory effects against *Candida albicans* secreted aspartic proteases (SAP) with IC_{50} values of 6.5 µg/ml [67].

Brassica rapa

The susceptibility of six microorganisms covering gram positive bacteria, gram negative bacteria and two fungi to the extracts and fractions of *Brassica rapa* was measured using cut plug method and the results compared with standard antibiotic gentamycin and the standard antifungal fluconazole. All the tested fractions and crude extracts revealed positive inhibitory effects against *Candida albicans*. Light petroleum fraction of roots showed somewhat strong antifungal activity against *Candida albicans* with MIC calculated as 12.5 mg/ml [68]. An 9.4-kDa antifungal peptide designated as campesin was isolated from seeds of the plant. It exerted an inhibitory action on mycelial growth including *Fusarium oxysporum* and *Mycosphaerella arachidicola*, with an IC_{50} of 5.1 microM and 4.4 microM, respectively. It also inhibited and the activity of HIV-1 reverse transcriptase with an IC_{50} of 3.2 microM. It demonstrated lysolecithin binding activity [69]. It was also known that arvelexin, one of the phytoalexins extracted from *Brassica rapa* possessed antifungal activity [70]. *Brassica rapa* was separated in seeds, stems-leaves, and roots, and then macerated with ethanol. *F. oxysporum* was seeded on PDA medium separately supplemented with each extract and radial growth was assessed after 6 days. All *Brassica rapa* extracts exhibited dose dependent antifungal activity at different levels. Root-derived extract showed inhibition percentages above 45% between 10 – 0.1 µg/µL. Stem-leaf and seed-derived extracts also showed reasonable inhibition (> 30% and > 35%, respectively) in the same concentration range [71].

Caesalpinia crista

The compound, α-(2-hydroxy-2-methylpropyl)-ω-(2-hydroxy-3-methylbut-2-en-1-yl) polymethylene, isolated from ethyl acetate leaf extract of *Caesalpinia crista* was evaluated against *Candida albicans* and *Rhodotorula sp.* using agar diffusion method. The compound exerted a concentration-dependent activity against tested yeast strains comparable to standards fluconazole and griseofulvin for *Candida albicans* and *Rhodotorula sp.* The inhibition zones was (IZ >20 mm) for *C. albicans* and *Rhodotorula sp* [72].

Calamintha graveolens

The essential oil (in 1:10 dilution, w/v mg/µl) exerted antifungal effects. A significant reduction in the Candida albicans growth was recorded (with antifungal zone measuring 20mm). The antifungal effects could be attributed to its hydrocarbon sesquiterpenes , germacrene and bicycle-germacrene contents [73].

Calendula officinalis

Both methanol and ethanol extracts of *Calendula officinalis* showed excellent antifungal activity against tested strains of fungi [74-76]. The essential oil of the flowers showed good potential antifungal activity (at 15 µl/disc) when tested against *Candida albicans (ATCC64548), Candida dubliniensis (ATCC777), Candida parapsilosis (ATCC22019), Candida glabrata(ATCC90030), Candida krusei (ATCC6258),* and yeast isolated from humans [77].

Calotropis procera

Antifungal and antibacterial activity of solvent extracts of *Calotropis procera* growing wild in Saudi Arabia were evaluated against *Candida albicans*. A bioassay-guided fractionation of the crude flavonoid fraction (Cf3) of methanol extract which showed the highest antimicrobial activity led to the isolation of four flavonoid glycosides as the bioactive constituents. Most of the isolated extracts showed antimicrobial activity against the test microorganisms, where the crude flavonoid fraction was the most active, diameter of inhibition zones ranged between 15.5 and 28.5 mm against the tested bacterial strains, while reached 30 mm against *Candida albicans* [78]. The differential antimycoses activities of chloroform, methanol and ethyl acetate extracts of *Calotropis procera* (50,100 and 150 mg/ml) were studied against *Trichophyton rubrum, Trichophyton tonsurans, Trichophyton mentagrophyte, Epidermophyton floccosum* and *Aspergillus.* Ethyl lactate extract produced the potent activity followed by chloroform extract, while methanol extract had no antifungal activity in all concentrations used in the study [79]. The osmotin purified from *Calotropis procera* latex, inhibited the spore germination of *Fusarium solani*. Osmotin interacted with the negatively charged large unilamellar vesicles (LUVs) of 1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-rac-1-glycerol (POPG), inducing vesicle permeabilization by the leakage of calcein. Osmotin induced the membrane permeabilization of spores and hyphae from *Fusarium solani*, allowing for propidium iodide uptake [80].

Capparis spinosa

The antifungal activities of ethanolic extract of (*Capparis spinosa* L.) was investigated *in vitro* against *Alternaria alternata, Fusarium oxysporum, Phoma destructiva, Rhizoctonia solani,* and *Sclerotium rolfsii* at concentrations of 0, 3, 6, and 9% (v/v). It produced concentration dependent fungal growth inhibition [81].

A monomeric protein with molecular mass of 38 kDa was purified from *C. spinosa* seeds. It inhibited HIV-1 reverse transcriptase and fungal mycelia growth without having hemogglutinating, ribonuclease, mitogenic or protease inhibitor properties. A novel dimeric 62-kDa lectin was also extracted from caper (*C. spinosa*) seeds, it also inhibited HIV-1 reverse trans-criptase and proliferation of both hepatoma HepG2 and breast cancer MCF-7 cells [82].

Capsella bursa-pastoris

Two novel antimicrobial peptides were isolated and characterized from the roots of shepherd's purse, *Capsella bursa-pastoris*. These antimicrobial peptides, named shepherin I and shepherin II, consist of 28 and 38 amino acids, respectively, and are glycine- and histidine-rich peptides. Shepherin I and shepherin II have 67.9% and 65.8% (mol/mol) glycine, respectively, and 28.6% and 21.1% (mol/mol) histidine, respectively. Both shepherins have a Gly-Gly-His motif. These antimicrobial peptides exhibit antimicrobial activity against Gram-negative bacteria and fungi [83].

Capsicum annum

The extracts of *Capsicum annum* showed antifungal activity against *A. niger* and *C. albicans* with inhibition zone diameter range of 10-16 mm/15*M*l [84-85].

Carum carvi

The antifungal screening of the essential oil of *Carum carvi* showed 100% inhibition of radial mycelial growth of all the test fungi at 100 ppm. The MIC and minimum fungicidal concentration (MFC) values were found to vary from 50-300 ppm and 200-400 ppm respectively [86].

Cassia occidentalis

Crude extracts of different parts (leaf, seed and pod) of *Cassia occidentalis* was examined for their antifungal activity against three fungi viz. *Candida albicans*,*Aspergillus clavatus* and *Aspergillus niger*. Antifungal activity of different plant parts in terms of minimal inhibitory concentration ranged between 200-1000 µg/ml. The extracts performed as good as or even better than the standard drugs nystatin and greseofulvin with exception of activity of leaf extracts against Aspergilli [85, 87].

Chenopodium album

Antifungal activity of methanol and n-hexane leaf, stem, root and inflorescence extracts of *Chenopodium album* (1, 2, 3 and 4% w/v) was investigated against *Macrophomina phaseolina*, a soil-borne fungal plant pathogen that has a broad host range and wide geographical distribution. The n-hexane extracts of *Chenopodium album* reduced fungal biomass by 60-94%[88]. The zone of growth inhibition of methanol and ethyl acetate extracts of the plant was 18.3mm against *Candida albicans* ATCC 18804 [89].

Chrozophora tinctoria

The crude methanol extract of the plant was tested against seven fungal strains (*Fusarium moniliformes, Fusarium solani, Aspergillus niger, Aspergillus fumigatus, Aspergillus flavus, Alternaria* sp. and *Mucor* sp.). The plant extracts showed low antifungal activity against all the seven fungal strains. The percentage inhibition in linear growth was 22.08± 2.2, 2.89± 2.61, 32.73±1, 23.48±2, 18.33± 3.3, 7.14± 3.3 and 28.26± 5.6 respectivily [90]. However, aqueous and methanolic extracts of *Chrozophora tinctoria* showed no antifungal activity against *Rhizoctonia solani, Fusarium oxysporum* and *Cochliobolus sativus* [91].

CONCLUSION

The paper reviewed the antifungal effects of the medicinal plants to open the door for their utilization in medical applications as a result of effectiveness and safety.

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