

PHCOG REV.: Review Article

Recent Herbal Trends against Fungal Infections: A Review

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ABSTRACT

Herbs have been one of the important and unique sources of medicines even since the dawn of human civilization. In spite of tremendous development in the field of allopathy during the 20th century, plants still remain one of the major sources of drug in the modern as well as traditional system of medicine throughout the world. Over 60% of all pharmaceuticals are plant-based. Plants and its phytoconstituents are used not only used to prevent but also used to cure various disorders. Various researches on plants all over the world either have been or have to be carried out for eradicating ailments. Most common of which is fungal infections, especially Mucosal Candidiasis caused by fungi *Candida albicans*. The incidence of fungal infections is increasing at an alarming rate, presenting an enormous challenge to healthcare professionals. This increase is directly related to the growing population of immunocompromised individuals, resulting from changes in medical practice such as the use of intensive chemotherapy and immunosuppressive drugs. The present study is a review on plants that have been found to have antifungal action against *Candida albicans*. Phytoconstituents isolated from various plants such as *Echinacea purpurea*, *Foeniculum vulgare* Miller, *Mentha piperita* L., *Citrus limon*, *Lycopodium cernuum*, *Nigella sativa*, *Pallavicinia lyellii* etc. had been investigated by various scientists and were found to have potent antifungal activity against *Candida albicans* and their various strains.

Keywords: Antifungal, *Candida albicans*, oropharyngeal candidiasis, vulvovaginal candidiasis

INTRODUCTION

Since time immemorial man has been using plant extracts to protect himself against several diseases and also to improve his health and life-style. No doubt, plants are serving several purposes whether health, nutrition, beauty or medicinal. With the development in techniques and recent researches, it has been proved that certain nutritive and non-nutritive chemicals in plants which are of very much importance to human diet possess healing properties. Plants and its phytoconstituents can also be used to treat fungal infections particularly Candidiasis such as oropharyngeal candidiasis, vulvovaginal candidiasis and others such as spirotrichosis, chromoblastomycosis, Tinea pedis etc. (1, 2)

With the increased use of antibiotics and immunosuppressive agents, fungal infections such as Candidiasis are becoming very-very common. Candidiasis is an opportunistic systemic fungal infection caused by fungus *Candida*, which occurs primarily when some aspect of the normal host defence is compromised. *Candida*, yeast like fungus, is commonly part of the normal flora of the skin, mouth, intestinal tract, and vagina and is presenting the oral cavity in 40% to 60% of the population. (3, 4) *Candida albicans* is the most commonly isolated species and is the species most likely to cause disease in humans. Other *Candida* species include *Candida tropicalis* (prevalent in immunosuppressed patients), *Candida krusei*, *Candida guilliermondii*, and *Candida parapsilosis* (of limited pathogenicity but particularly associated with infection of indwelling vascular access devices) (5)

Candidiasis can be of two types superficial (which occurs at outermost layers of skin, nails, hair, mucous membranes) and systemic candidiasis (which occurs at deep tissue invasion of one or more internal organs). Both of them occurs more frequently because of increased use of antibiotics and immunosuppressive agents and such advances in medical management as chemotherapy, organ transplantation,

parenteral nutrition, and invasive surgical procedures.(6) Such infections are life threatening and are associated with high rates of death. Because of the growing population of immunocompromised individuals, the frequency of systemic fungal infections is increasing significantly. (1, 2)

Various topical and systemic agents are available to treat patients suffering from candidiasis, but optimal management can be elusive. Due to side effects of synthetic drugs now-a-days herbal formulations are becoming much popular. Indian Vaidyas, Hakims as well as tribal people have developed and recorded the knowledge of the various uses. Various scientists and research workers have also reported a lot of scientific work on this disorder.

Research Envisaged on Anti-candidal Activity of Active Constituent of Plants

Anticandidal activity of plants containing Volatile oil

Drugs containing volatile oil shows activity against fungal infections as shown by Ezzat et al., (7). He showed inhibitory actions of essential oil of *Foeniculum vulgare* Miller, *Mentha piperita* L. and *Citrus limon*. While, methanol extracts of both leaves and male cones of the conifer *Eucalyptus occidentalis* and *Thuja orientalis* had an inhibitory influence on the growth by two tests (cut plug and filter paper disc assay). A lot of scientific work narrates antifungal activity against *Candida albicans*. Manohar et al., (8) analyzed *Origanum* commercial oil against *Candida albicans*. Inhibition of secreted aspartic proteases (SAP) of *Candida albicans* have been shown to be a major virulence factor in *Candida* infections. As we proceed further, the effect of an aqueous extract of *Nigella sativa* seeds was proposed on candidiasis in mice by Khan et al.,(9) in which an intravenous inoculum of *Candida albicans* produced colonies of the organism in the liver, spleen and kidneys was prepared. Treatment of mice with the plant extract (6.6 mL/kg equivalent to 5 mg of

estimated protein), once daily for 3 days 24 h after the inoculation caused a considerable inhibitory effect on the growth of the organism in all organs studied.

Comparative study was also proposed for essential oils in which essential oil composition and antifungal effect of *Foeniculum vulgare ssp. Piperitum* fruit oils obtained during different vegetation was researched and compared by Ozcan et al., (10). The chemical composition of the flower and unripe and ripe fruits from *Foeniculum vulgare ssp. piperitum* has been examined by gas chromatography and gas chromatography-mass spectrometry.

Further, Antifungal properties of *Ocimum gratissimum* essential oil (ethyl cinnamate Chemotype) was investigated by Dubey et al., (11). Recent research on its essential oils showed five chemotypes. An Indian chemotype, with a high level of ethyl cinnamate, presents, in vitro, an interesting spectrum of antifungal properties. Minimal inhibitory concentration of ethyl cinnamate chemotype of *O. gratissimum* essential oil and of its main constituents was found against *Scopulariopsis brevicaulisa*, *Aspergillus fumigatus*, *Candida albicans* etc. Radulovi et al., (12) demonstrated composition and antimicrobial activity of *Equisetum arvense* L. essential oil. They identified twenty-five volatile constituents of essential oil using GC, GC/MS and ¹³C-NMR out of which Hexahydrofarnesyl acetone (18.34%), *cis*-geranyl acetone (13.74%), thymol (12.09%) and *trans*-phytol (10.06%) were the major constituents. Evaluation of the antimicrobial activity of the oil was carried out against a panel of microorganisms (bacteria: *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Candida albicans* etc).

Nakamura et al., (13) showed in vitro activity of essential oil from *Ocimum gratissimum* L. against four *Candida* species i.e. *Candida albicans*, *Candida krusei*, *Candida parapsilosis*, and *Candida tropicalis*. Transmission and scanning electron microscopy and negative staining in light microscopy were performed to reveal the effects of the essential oil on the morphology of these yeasts. Analysis of the ultra structure of the yeast cells revealed changes in the cell wall and in the morphology of some sub cellular organelles. Bud formation in the yeasts was impaired in treated cells.

Anticandidal low molecular compounds from higher plants with special reference to compounds from essential oils was demonstrated by Pauli et al., (14). The most active low molecular weight compounds from higher plants against *Candida* species are compiled from a database of antimicrobials (Amicbase) to find out new hints on their mechanism of action in which the majority (55%) of essential oils is utilized in food industry for the production of aroma extracts.

Skocibusic et al., (15) carried out phytochemical analysis(GC/MS analysis) and *in vitro* antimicrobial activity of two *Satureja* Species essential oils (aerial parts of *Satureja montana* L. and *Satureja cuneifolia* Ten.).The major compound of *S. montana* oil was the phenolic monoterpene carvacrol (45.7%). and volatile oil of *S. cuneifolia* was characterized as β -cubebene (8.7%), limonene (8.3%), α -pinene (6.9%), spathulenol and β -caryophyllene.

The formulation of an effective topical antibacterial product containing *Ocimum gratissimum* leaf essential oil was demonstrated by Orafiya et al.,(16) Liquid and semisolid formulations of the oil designed in a variety of bases were evaluated by agar diffusion assay against type strains and clinical isolates from boil, wound and pimples. Remarkable antibacterial effects, higher than those of commercial antiseptic products, were demonstrated at 2% *Ocimum* oil concentration in some bases.

Woollard et al., (17) isolated the only known natural source of the volatile bioactive compounds bullatenone and 4-methyl-1-phenylpentane-1,3-dione from endemic shrub *Lophomyrtus bullata* (Myrtaceae) which showed antifungal activity against *Candida albicans* and *Cladosporium resinae*, and an oil from the 4-methyl-1-phenylpentane-1,3-dione 2 chemotype showed antibacterial activity against *Bacillus subtilis*. Giordani et al. (18) found out compositions and antifungal activities of essential oils of some 10 Algerian aromatic plants. The highest efficiency was obtained with the essential oil from *Thymus numidicus* which showed antifungal effect 1357 fold stronger than that measured with amphotericin B.

Schwartz et al. (19) tested antibacterial and antifungal activity of ten essential oils against a range of vaginal bacterial and fungal strains isolated from existing vaginal infections including *Atopobium vaginae*, *Gardnerella vaginalis*, *Bacteroides vulgatus*, *Candida albicans*, *Candida glabrata*, *Candida tropicalis*. In overall, lemongrass, palmarosa, lavender and rose scented geranium were the most potent oils in the inhibition of pathogenic bacteria and fungi.

Tan et al. (20) isolated various constituents such as β -sitosterol, stigmasterol and daucosterol from the roots of *Inula racemosa* and elucidated their structures by a combination of spectral methods (IR, EIMS, ¹H and ¹³C NMR, DEPT, COSY, NOESY and HETCOR). All isolates were subjected to antifungal tests and found to be active against the human pathogenic fungi, *Aspergillus flavus*, *A. niger*, *Geotrichum candidum*, *Candida tropicalis* and *C. albicans* at concentrations of 50, 50, 25, 25 and 25 μ g/ml, respectively.

Anticandidal activity of plants containing Carbohydrates and Proteins

Further, Steinmuller et al., (21) studied about Polysaccharides isolated from plant cell cultures of *Echinacea purpurea* which enhances the resistance of immunosuppressed mice against systemic infections with *Candida albicans* and *Listeria monocytogenes*. In this study, they investigated the influence of polysaccharides on the nonspecific immunity in immunodeficient mice which have been shown to activate human and murine phagocytes. Following this Roesler et al., (22) found out the application of purified polysaccharides from cell cultures of the plant *Echinacea purpurea* and investigated their ability to enhance phagocytes activities regarding nonspecific immunity in vitro and in vivo against *Candida albicans*.

Antifungal activity was shown by Hejgaard et al., (23) in which he associated 2 immunochemically distinct proteins, protein R and S (M_r 23 kDa; pI 9-10), which were isolated in pure form from barley grain. The proteins inhibit growth of

i.a. *Trichoderma viride* and *Candida albicans* in microtiter plate assays and act synergistically with barley grain chitinase.

Lindquist et al., (24) isolated five novel benzenoids, polycarpamines A-E (1-5), with rare, sulfur-containing functional groups, from the solitary marine ascidian *Polycarpa auzata* in which Polycarpamine B (2) exhibited significant antifungal activity *in vitro* against *Saccharomyces cerevisiae* and *Candida albicans*. After this Costa et al., (25) demonstrated antifungal activity of essential oil obtained from the hydro distillation of *Eugenia dysenterica* leaves using the agar dilution method against eight strains of *Candida albicans* isolated from HIV-infected individuals with candidosis or cryptococcal meningitis. It was found that MICs $\geq 3.12 \mu\text{g/ml}$ for 91.6, 50 and 30% of all *Cryptococcus* strains in relation of amphotericin B, fluconazole and itraconazole, respectively.

Anticandidal activity of plants containing Terpenoids

A lot of scientific work narrates that many plants and their isolates containing terpenoids possess antifungal activity as suggested by Ancri et al., (26) who showed antimicrobial properties of allicin from garlic particularly antifungal activity against *C. albicans*. Regarding this Zhang et al., (27) proposed a new approach in the control of candidiasis. Activity-guided fractionation of an ethanol extract of *Lycopodium cernuum* for *Candida albicans* secreted aspartic proteases (SAP) inhibition resulted in the identification of six new and four known serratene triterpenes.

Magwa et al., (28) isolated α -pinene, camphene, β -pinene, α -terpinene, *O*-cymene, limonene, 1,8-cineole, α -terpinene etc. from *Sesuvium portulacastrum* using GC-MS analysis, and used mycelium growth inhibition method for the antifungal testing against *Candida albicans*, *Aspergillus niger*, *Aspergillus flavus* and *Penicillium notatum*. Further Meng et al., (29) isolated three highly oxygenated guaianolides from the aerial parts of *Ajania fruticulosa* along with 17 known phytochemicals including a triterpene (α -amyrin), two plant sterols (β -sitosterol, daucosterol), four flavonoids (axillaridin, centaureidin, santin and 5,7,4'-trihydroxy-3,3'-dimethoxyflavone), and ten sesquiterpenes. Their structures were elucidated by a combination of spectroscopic methods (EIMS, HREIMS, COSY, HMQC, HMBC and NOESY). Antifungal bioassay of all isolates was performed.

Koo et al., (30) proposed antimicrobial activity of *Arnica montana* and propolis against *Candida albicans* – NTCC 3736, by the agar diffusion method and the zones of growth inhibition were measured. Propolis extract showed *in vitro* antibacterial activity, inhibition of cell adherence and inhibition of water-insoluble glucan formation, while the *Arnica* extract was only slightly active in those three conditions. Another antifungal activity was carried out by Ioset et al. (31) who isolated three new meroterpenoid naphthoquinones, the known cordiaquinone B and a new naphthoxirene from the roots of *Cordia linnaei*. Their structures were established by spectrometric methods including EI, D/CI and FAB mass spectrometry, ^1H , ^{13}C and 2D NMR experiments.

Anticandidal activity of plants containing resins

Other important drugs such as turmeric also induct predominant anti-fungal activity as reported by Grisanapan et al., (32). In one study, it was observed that its extract has fungicidal action against *C. albicans* MTCC-183 and *Cryptococcus neoformans* MTCC-1347 strains. Another important investigation carried out by Kapoor et al., (33) who reported that fresh juice and extract of *Curcuma longa* arrest the growth of *A. nigar* and *Penicillium digitatum* in usual concentration. Behura et al., (34) reported that essential oil of *Curcuma longa* leaf has anti-fungal action as similar as standard fungicides like cabendazim and mancozeb. Venugopal et al., (35) reported that curcuma oil exhibits excellent insect repellent property even at 1% concentration in water. Apisariyakul et al., (36) showed significant antifungal activity of turmeric oil extracted from *Curcuma longa*.

Anticandidal activity of plants containing Glycosides

Another group of scientists demonstrated antifungal activity of phytoconstituents such as glycosides. A. Favel1 et al., (37) isolated steroidal glycosides named alexin from crude extract of *Yucca gloriosa* L. and investigated *in vitro* antifungal activity against a panel of human pathogenic fungi, yeasts as well as dermatophytes and filamentous species. They found that alexin had a broad spectrum of antifungal activity and found to reside entirely in the spirostanoid fraction. After this Sautour et al., (38) did phytochemical investigation of the rhizome of *Dioscorea dumetorum* and led to the isolation by several chromatographic steps on normal and reversed phase silica gel of a new ecdysteroid, (20R)-5 β ,11 α ,20-trihydroxyecdysone (1), and two known ecdysteroids, ajugasterone C (2) and herkesterone (3). These compounds were however devoid of antifungal activity against three *Candida* species.

Further Agnese et al., (39) showed antifungal activity of the ethanolic extract of *Adesmia aegiceras* against *Candida albicans* by the agar-well diffusion method and revealed quercetin, isorhamnetin-3-rutinoside, isovitexin, pinitol and chlorogenic acid as its main components from alcoholic extract. This indicated the potential usefulness of the *A. aegiceras* extract as a microbiostatic, antiseptic or disinfectant agent.

Another report was given by Agrawal et al., (40) who isolated Rhein, physcion, aloe-emodin and chrysophanol from *Rheum emodi* rhizomes which exhibited antifungal activity against *Candida albicans*, *Cryptococcus neoformans*, *Trichophyton mentagrophytes* and *Aspergillus fumigatus* (MIC 25-250 $\mu\text{g/ml}$).

Sardari et al., (41) proposed a molecule called as Angelicin, a naturally occurring furanocoumarin, that showed antifungal activity against *Candida albicans*, and was considered as a lead structure for a group of synthetic coumarins.

Anticandidal activity of plants containing Alkaloids

Arenosclerins A-C and haliclonyclamine E are new tetracyclic alkyloperidine alkaloids isolated from marine sponge *Arenosclera brasiliensis*. This study was carried out by Torress et al., (42) who further subjected them to antimicrobial and cytotoxic bioassays.

Anticandidal activity of plants containing fixed oils

Significant antifungal activity had been demonstrated by certain fixed oils as shown by Sairam et al. (43) who found out the efficacy of NIM-76, a spermicidal fraction from neem oil, and investigated its antimicrobial action against certain fungi and Polio virus as compared to whole neem oil as exhibited in vero cell lines. It also protected mice from systemic candidiasis as revealed by enhanced % survival and reduced colony forming units of *C. albicans* in various tissues.

Anticandidal activity of a group of indigenous plants of certain regions

A vast group of scientists investigated antifungal activity on indigenous group of plants growing in their respective regions. Likewise, Sterer et al., (44) demonstrated the antimicrobial activity of the herbal formulation ingredients (i.e. sage, Echinacea, Lavender and Mastic gum) against three oral pathogens (*Streptococcus mutans*, *Porphyromonas gingivalis* and *Candida albicans*) by the agar diffusion test. The antimicrobial activity of crude ethanolic extracts of 16 Siberian medicinal plants was tested against five species of microorganisms: *Bacillus cereus*, *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Candida albicans* by Kokoska et al., (45). An extensive research on African plants speaks volumes regarding antifungal activity. Like, screening of traditionally used South African plants for antifungal activity against *Candida albicans* was done by Motsei et al., (46) Twenty-four South African medicinal plants were screened against *Candida albicans* standard strain ATCC 10231 and two clinical isolates from a 5-month-old baby and an adult, in an attempt to find a traditional remedy to treat oral candidiasis, which is prevalent in HIV-patients. Hamza et al.,(47) found out antifungal activity of some Tanzanian plants, used traditionally for the treatment of fungal infections against *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, *Candida krusei* and *Cryptococcus neoformans*.

Furtherly, Finnish plant extract have also shown to be potent antimicrobial activity. Antimicrobial effects of Finnish plant extracts containing flavonoids and other phenolic compounds was investigated by Rauha et al.,(48) in which Flavone, quercetin and naringenin were effective in inhibiting the growth of the organisms particularly *Candida albicans*. The antibacterial and antifungal activity of ten essential oils was tested by Schwiertz et al., (49), against a range of vaginal bacterial and fungal strains isolated from existing vaginal infections including *Atopobium vaginae*, *Gardnerella vaginalis*, *Bacteroides vulgatus*, *Streptococcus agalactiae* and *Candida albicans*.

South Indian plants have also shown to be potent antifungal like medicinal action. In this Vaijayanthimala et al.,(50) studied the anticandidal activity of 20 household South Indian medicinal plants and/or plant products using 30 *Candida albicans* isolates obtained from vaginal candidiasis patients of Rajah Muthiah Medical College and Hospital and compared with the anticandidal activity of garlic.

Steenkamp et al.,(51) prepared crude methanol and water extracts of 32 plant species, used for the treatment of

infectious diseases in Venda and were screened for in vitro activity against *Candida albicans* standard strain (ATCC 10231) and five clinical isolates. Gracilene Schmourlo et al., (52) screened antifungal agents using ethanol precipitations and bioautography of medicinal and food plants against skin diseases by the Brazilian population.

Utsunomiya et al.,(53) studied that Glycyrrhizin improves the resistance of MAIDS Mice to Opportunistic Infection of *Candida albicans* through the Modulation of MAIDS-Associated Type 2 T Cell Responses. Rojas et al., (54) evaluated Mexican traditional medicine for the treatment of respiratory infections for potential antimicrobial activity against *Candida albicans*.

Rosado-Vallado et al., (55) showed extracts of six Fabaceae species, traditionally used in Mayan medicine for the treatment of diarrhoea and eye infections, were tested for in vitro antimicrobial activity against candidiasis.

Ahmad et al., (56) studied ethanolic extracts of 45 Indian medicinal plants traditionally used in medicine and found out their antimicrobial activity against certain drug-resistant bacteria and a yeast *Candida albicans* of clinical origin. Of these, 40 plant extracts, 24 plants showed varied levels of antimicrobial activity against one or more test bacteria anticandidal activity while overall, broad-spectrum antimicrobial activity was observed in 12 plants (*L. inermis*, *Eucalyptus* sp., *H. antidysenterica*, *H. indicus*, *C. equisetifolia*, *T. belerica*, *T. chebula*, *E. officinalis*, *C. sinensis*, *S. aromaticum* and *P. granatum*). No correlation was observed between susceptibility of test strains with plant extracts and antibiotic resistance behavior of the microbial strains.

Extracts of six ethnobotanically selected medicinal plants (*Anredera cordifolia*, *Elaeodendron transvaalense*, *Elephantorrhiza burkei*, *Senna petersiana*, *Terminalia sericea* and *Rauvolfia caffra*) used traditionally to treat sexually transmitted diseases (STD's) were investigated by Tshikalange et al., (57), for antibacterial activity using the agar dilution method. Of the six collected, *Terminalia sericea*, *Senna petersiana* and *Anredera cordifolia* were also investigated for cytotoxicity. The phytochemical studies on *enenna petersiana* resulted in the isolation of luteolin, which also showed antimicrobial activity.

Vonshak et al., (58) screened South Indian Medicinal Plants for antifungal activity against cutaneous pathogens. In this study, twenty-eight South Indian medicinal plants were screened for their anti-fungal activity against six species of fungi (*Trichophyton mentagrophytes*, *T. rubrum*, *T. soudanense*, *Candida albicans*, *Torulopsis glabrata*, and *C. krusei*). Three plant species extracts, *Celastrus paniculatus*, *Eriodendron anfractuosum* and *Ficus glomerata* showed inhibitory activity. An aqueous extract of galls of *Terminalia chebula* showed inhibitory effects on three dermatophytes (*Trichophyton* spp.) and three yeasts (*Candida* spp.).

Desta et al., (59) investigated a total of 315 direct aqueous extracts/fractions from 63 traditionally used Ethiopian plants and performed their antimicrobial screening using known strains of *Staphylococcus aureus*, *Salmonella gallinarum*, *Escherichia coli*, *Candida albicans* etc. These findings confirm traditional therapeutic claims for aqueous dosage forms of

these herbs and relative susceptibility of the test organisms to the five types of extracts/fractions indicated a decreasing rank order of *S. aureus*, *P. aeruginosa*, *C. albicans*, *S. gallinarum*, *E. coli*, *K. pneumoniae* and *P. vulgaris*.

Antimicrobial activity of South African *Podocarpus* species was *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Candida albicans* etc was investigated by Abdillahi et al., (60) and all species exhibited antimicrobial activity with MIC values of less than 1 mg/ml.

Trakranrungsie et al., (61) demonstrated ethnoveterinary study for antidermatophytic activity of *Piper betle*, *Alpinia galanga* and *Allium ascalonicum* extracts in vitro. Among the extracts tested, *P. betle* exhibited more effective antifungal properties and has potential therapeutic value for treatment of dermatophytosis. Subsequently, Garza et al., (62) screened antifungal activity of plants from the northeast of Mexico against *Candida albicans*, *Aspergillus fumigatus*, *Histoplasma capsulatum*, and *Coccidioides immitis*. Ten hydroalcoholic extracts from the 15 plants evaluated showed antifungal activity against at least one of these fungi. Following this, a differential extraction was conducted with solvents of different polarities, and 16 extracts showed activity ranging from 16 to 125 µg/mL against the different fungi.

Kumar et al., (63) searched for antibacterial and antifungal agents from selected Indian medicinal plants like *Dorema ammoniacum*, *Sphaeranthus indicus*, *Dracaena cinnabari*, *Mallotus philippinensis*, *Jatropha gossypifolia*, *Aristolochia indica*, *Lantana camara*, *Nardostachys jatamansi*, *Randia dumetorum* and *Cassia fistula* exhibited significant antimicrobial activity and properties that support folkloric use in the treatment of some diseases as broad-spectrum antimicrobial agents. This probably explains the use of these plants by the indigenous people against a number of infections.

Buwa et al., (64) used extracts of 13 plants used in South Africa for the treatment of venereal diseases and screened them for antibacterial and antifungal activity. In antifungal screening, good activity was shown by the ethanolic extracts of *Bersama lucens* and *Harpephyllum caffrum*. Only in the case of *Harpephyllum caffrum* did aqueous extracts have activity against *Candida albicans*. Navarro et al., (65) investigated Eighteen plant extracts from nine traditional Mexican medicinal plants and tested for antifungal activity against two dermatophyte fungal species (*Trichophyton mentagrophytes* and *Trichophyton rubrum*), one non-dermatophyte (*Aspergillus niger*), and one yeast (*Candida albicans*) in which the strongest effect was manifested by the hexane extracts from *Eupatorium aschenbornianum* and *Sedum oxypetalum*.

Lopez et al., (66) detected strong antiviral and antimicrobial activities in methanolic extracts of 24 plants used medicinally in the treatment of skin infections in four different regions of Colombia. Anti-*Candida* activity was observed for *Piper lanceaeifolium* HBK. and *Juglans neotropica* Diels. Omar et al., (67) isolated wood and bark extracts of 14 eastern North American hardwood tree species which were used traditionally as medicine by First Nation's people and screened them for antifungal with six strains of fungi. The

bark extract from *Juglans cinerea* had the broadest spectrum of activities against *Candida albicans*, *Saccharomyces cerevisiae*, *Aspergillus fumigatus* etc.

Mahasneh et al. (68) conducted research on the whole aerial parts of nine plants and concluded that its extracts in various solvents exhibited variable degrees of antimicrobial activity against four bacterial and three fungal species. Furthermore, higher antibacterial activity was observed though low to moderate compared with streptomycin and very comparable with chloramphenicol.

Miscellaneous

S.K. Lee et al., (69) investigated the antibacterial and antifungal activities of pinosylvin (3, 5-dihydroxy-trans-stilbene), a constituent of pine, and compared it with positive control resveratrol (3, 5, 4'-trihydroxy-trans-stilbene). Pinosylvin exhibited more potent growth inhibitory activity against *Candida albicans* and *Saccharomyces cerevisiae*. Desmethyl isoenecalin and 5-hydroxy-6-acetyl-2-hydroxymethyl-2-methyl chromene isolated from *Blepharispermum subsessile* rhizomes were shown to have antifungal activity against *Candida albicans* and *Cryptococcus neoformans* (MIC 25-250 µg/ml). This study was carried out by S.K.Agrawal et al., (70)

S. Subhisha et al., (71) studied the efficacy of the active fraction of *Pallavicinia lyellii*, a liverwort against aspergillosis caused by *A. fumigatus* in immuno-compromised mice. Thus, *P. lyellii* is likely to be a suitable material for developing invaluable antifungal activity. Torras et al., (72) demonstrated antimicrobial activity of Pycnogenol which is a standardized extract of *Pinus pinaster* bark, against 23 different pathogenic prokaryotic (gram-positive and gram-negative) and eukaryotic (yeast and fungi) microorganisms. The positive results for antifungal activity conform with clinical oral health care studies describing the prevention of plaque formation and the clearance of Candidiasis by Pycnogenol. After this Gentil et al., (73) evaluated in vitro antibacterial activity of *Arctium lappa* as a phytotherapeutic agent used in intracanal dressings. This study evaluated the antibacterial activity of a phytotherapeutic agent prepared from an ethyl acetate fraction (AcOEt) extracted from *Arctium lappa*. Twenty-seven maxillary canines were instrumented, sterilized and inoculated with a mixed bacterial suspension of *Pseudomonas aeruginosa*, *Escherichia coli*, *Lactobacillus acidophilus*, *Streptococcus mutans* and *Candida albicans*.

Further, Agnihotri et al., (74) isolated from the leaves of *Nelumbo nucifera* (an aquatic plant), one new compound, 24(R)-ethylcholest-6-ene-5 α -ol-3-O-B-d-glucopyranoside (1), along with 11 known metabolites (2-12) and identify them by spectroscopic methods including 1D- and 2 NMR. Antifungal activity was found out for (R)-roemerine (IC₅₀/MIC = 4.5/10 µg/mL against *Candida albicans*). None of the compounds were cytotoxic to Vero cells up to a concentration of 23.8 µg/mL.

Shai et al., (75) isolated Lupeol, betulinic acid, ursolic acid and 2 α -hydroxyursolic acid from *Curtisia dentata* leaves. Betulinic acid, ursolic acid and 2 α -hydroxyursolic acid appreciably inhibited fungal growth with MIC values ranging

from 8 to 63 µg/mL. This study provides information on the antimicrobial compounds of this species, as well as a preliminary rationale for the use of *Curtisia dentata* in traditional South African medicine.

Garg et al., (76) carried out in vitro activity of terbinafine, a new chemical class of antimycotic compounds against Indian clinical isolates of *Candida albicans* and non-*albicans* using a macrodilution method. The aim of this study was to determine the anti *Candida* activity of terbinafine compared with amphotericin, fluconazole, ketoconazole and itraconazole.

Singh et al., (77) studied antimicrobial potential of *Plagiochasma appendiculatum* against a wide range of microorganisms and validated the ethno therapeutic claims of the plant in skin diseases, wound healing activity (wound contraction and increased tensile strength) besides antioxidant activity (by inhibiting lipid peroxidation and increase in the Superoxide Dismutase (SOD) and Catalase activity.)

Sisti et al., (78) found out the antifungal activity of fresh, aqueous *Brassica oleracea* var. *botrytis* juice against *Candida albicans* and other pathogenic fungi. The juice was found to be effective both in inhibiting the growth of blastoconidia and reducing the appearance of *C. albicans* germ tubes.

Somchit et al., (79) tested Crude ethanol and water extract of leaves and barks from *Cassia alata* in vitro against fungi, (*Aspergillus fumigatus* and *Microsporum canis*), yeast (*Candida albicans*) and bacteria (*Staphylococcus aureus* and *Escherichia coli*). *C. albicans* showed concentration-dependent susceptibility towards both the ethanol and water extracts from the barks, but resistant towards the extracts of leaves and concluded that this plant has antimicrobial activity which is as potent as standard antimicrobial drugs against certain microorganisms.

Giordani et al., (80) found out in vitro susceptibility of *Candida albicans* to ketoconazole and *Euphorbia characias* latex alone or in combination was tested using the macrobroth dilution method which shows a synergistic effect is therefore obtained between ketoconazole on the one hand and two concentrations of *Euphorbia characias* latex. Guntern et al., (81) investigated two new benzoquinones, heliotropinones A and B, from the aerial parts of *Heliotropium ovalifolium*. Their structures were elucidated by spectrometric methods including high resolution electrospray ionization (ESI-HR), EI mass spectrometry, ¹H, ¹³C and 2D NMR experiments and both of them demonstrated antifungal activities against *Cladosporium cucumerinum* and *Candida albicans*.

Carpinella et al., (82) investigated that the ethanol extract of *Melia azedarach* ripe fruits showed fungistatic (MIC 50-300 mg/ml) and fungicidal (MFC 60-500 mg/ml) against *Aspergillus flavus*, *Fusarium moniliforme*, *Microsporum canis* and *Candida albicans*

Kujumgiev et al., (83) demonstrated propolis samples from different geographic origins and investigated for their antibacterial (against *Staphylococcus aureus* and *Escherichia coli*), antifungal (against *Candida albicans*) and antiviral (against Avian influenza virus) activities. It seems that

propolis has general pharmacological value as a natural mixture and not as a source of new powerful antimicrobial, antifungal and antiviral compounds. Khan et al., (84) exhibited a wider spectrum of antibacterial and antifungal activity of the leaves, stem bark, stem heart wood, root and tubers of *Angiopteris evecta* with various solvents in which dichloromethane and ethyl acetate fractions of the leaves and stem bark were particularly good and were the only fractions exhibiting antifungal activity.

Ajaiyeoba et al., (85) screened for in vitro antifungal activity for crude extracts obtained from the leaves, stem bark and roots of *Ritchiea capparoides* var. *longipedicellata* using the agar tube dilution method. Griseofulvin was included as a reference compound and methanol as the control and preliminary cytotoxicity tests were done with the four extracts using the larvae of the brine shrimp, *Artemia salina*. Karlowsky et al., (86) found out a new compound BMS-181184 which is a water-soluble derivative of the pradimicin group and have antifungal activity. In vitro activities of BMS-181184 and comparator agents' amphotericin B, 5-fluorocytosine, fluconazole, and ketoconazole against 184 systemic fungal isolates collected at the Health Sciences Centre in Winnipeg, Canada, between 1987 and 1995.

Ma et al., (87) found out two new prenylated chromones, eriosematins D and E, which have been isolated from a dichloromethane extract of the roots of *Eriosema tuberosum*. Both chromones exhibited antifungal activity against *Cladosporium cucumerinum* and *Candida albicans* in TLC bioautographic assays.

LC-UV-mass spectrometry and bioassay co-directed fractionation of an aqueous acetone extract of the roots of *Gentiana macrophylla* gave three new chromene derivatives and two novel and six known secoiridoids, along with kurarinone, kushenol I, β-sitosterol, stigmaterol, daucosterol, β-sitosterol-3-O-gentiobioside, α-amyirin, oleanolic acid, isovitexin, gentiobiose and methyl 2-hydroxy-3-(1-β-D-glucopyranosyl)oxybenzoate which shows antifungal activity as demonstrated by Tan et al., (88)

Lastly, Tan et al., (89) carried out the fractionation of an aqueous acetone extract of the whole herb of *Gentiana algida* and gave one new [2'-(*o,m*-hydroxybenzyl)sweroside] and five known secoiridoids, together with anofinic acid, fomannoxin acid, sitosterol, daucosterol, stigmaterol, oleanolic acid, orientin and gentianose which have antifungal activity against the human pathogenic yeast *Candida albicans*.

Conclusion

Present article highlight the recent researches of active constituents of various plants against fungal infections particularly caused by *Candida albicans*. Although, plants have enormous potential not only to prevent diseases but also to cure dreadful disorders like fungal infections. *Candida albicans* is one of the most notorious fungi and allopathic medicines available commercially in the market are not satisfactory and have got various contraindications and side effects. Therefore, finding a perfect treatment that too in herbalism for fungal infections (either systemic or superficial) is a great challenge in itself. Application of tissue culture techniques can play an important role to increase the

percentage of its therapeutically active phytoconstituents. Recent researches and market report reveals that the maximum potential of various rare plants in external applications and for the treatment of some common fungal infections.

Various plants and their phytoconstituents have been used to eradicate not only *Candida albican* but also other species of candida such as *Candida tropicalis* (prevalent in immunosuppressed patients), *Candida krusei*, *Candida guilliermondii*, and *Candida parapsilosis* (of limited pathogenicity but particularly associated with infection of indwelling vascular access devices).

So, it is required to carryout pinpoint study related to such type of dangerous infections. There is a need to exploit maximum potential in the field of medicinal and pharmaceutical sciences for novel and fruitful application, because herbal drugs are holistic gift of nature.

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