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Review Article

ANTI-*CANDIDA* ACTIVITY OF MEDICINAL PLANTS. A REVIEW

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ABSTRACT

Due to the increasing development of drug resistance in human pathogens as well as the appearance of undesirable effect of certain antimicrobial agents, there is a need to search for new antifungal agents without toxicity and side effects. Although a large number of antimicrobial agents have been discovered, pathogenic microorganisms are constantly developing resistance to these agents. Therefore it is necessary to search for more effective and less toxic novel antifungal agents that would overcome these disadvantages. *C. albicans* is notorious for causing candidiasis. In order to alleviate the problem of reduced availability of drugs needed to treat candidiasis, traditional medicine derived from plants are still being used in different parts of the world. Hence, the present review is a compilation of updated information on plants with anti-*Candida* properties.

Keywords: Candidiasis, Anti-*Candida* Activity, Medicinal plants.

INTRODUCTION

The frequency of life-threatening infections caused by pathogenic microorganisms has increased worldwide, becoming an important cause of morbidity and mortality in immuno compromised patients in developing countries [1]. Although a large number of antimicrobial agents have been discovered, pathogenic microorganisms are constantly developing resistance to these agents [2]. However, since many of the available antifungal drugs have undesirable side effects or are very toxic, produce recurrence, show drug-drug interactions or lead to the development of resistance, some shows ineffectiveness [3] and have become therefore less successful in therapeutic strategies. Therefore it is necessary to search for more effective and less toxic novel antifungal agents that would overcome these disadvantages. An important group of the skin pathogens are the fungi, among which dermatophytes and *Candida* spp. are prominent [4, 5]. Under certain circumstances, usually associated with a compromised host immune system, *C. albicans* and related species can become pathogenic, causing oral, vaginal and/or systemic candidiasis [6]. Around 75% of adult women have at least one episode of vulvovaginal candidiasis (VVC) during their life, with prevalence of *C. albicans* in 70–90% [7]. *C. albicans* is notorious for causing candidiasis, it can affect the oesophagus with the potential of becoming systemic, causing a much more serious condition, afungemia called candidemia [8, 9]. It also causes a variety of infections that range from non-life threatening mucosal candidiasis like vaginal yeast infections, thrush, skin and diaper rash to lethal disseminated candidiasis in those with compromised immune systems who have an implantable medical device such as a pacemaker or artificial joint, or who use broad-spectrum antibiotics [10, 11, 12]. *C. albicans* infections faces a number of problems including limited number of effective antifungal agents, toxicity of the available antifungal agents, resistance of *Candida* to commonly used antifungals, relapse of *Candida* infections and non-cost effective antifungal agents [13]. In order to alleviate the problem of reduced availability of drugs needed to treat candidiasis, traditional medicine derived from plants are still being used [14]. This prompted the search for novel and active anti-*C. albicans* agents from plant sources.

Medicinal plants are renewable in nature unlike the synthetic drugs that are obtained from non-renewable sources of basic raw materials such as fossil sources and petrochemicals [15]. Due to all these advantages, plants continue to be a major source of new lead compounds. Nowadays, the indiscriminate use of commercial antimicrobial drugs has caused multiple drug resistance in human pathogenic microorganisms [16]. This situation forced scientists to search for new and effective antimicrobial agents to replace the current regimens [17]. Hence, the present review is an attempt for the compilation of updated information on plants with anti-*Candida* properties.

Euphorbia hirta L.

A transmission electron microscopy (TEM) study of the diversity of *C. albicans* cells induced by *E. hirta* leaf extract in vitro was studied to determine the major changes in the microstructure of *C. albicans* after treatment with *E. hirta* leaf extract. It was found that the main abnormalities were the alterations in morphology, lysis and complete collapse of the yeast cells after 36 h of exposure to the extract. Whereas the control (untreated) cultures showed a typical morphology of *Candida* with a uniform central density, typically structured nucleus, and a cytoplasm with several elements of endomembrane system and enveloped by a regular, intact cell wall. The significant antifungal activity shown by this methanol extract of *E. hirta* suggests its potential against infections caused by *C. albicans* [18]. Previous studies showed that the methanol extract of *E. hirta* possessed a good in vitro antifungal activity against *C. albicans* with 21 mm zone of inhibition, a minimum inhibitory concentration (MIC) value of 3.125 mg/mL, and the time kill study revealed a fungicidal effect with 1 and 2 MIC values of the plant extract [19]. Longer exposure to the extract inhibits the total growth of *C. albicans*. Seed extract of *E. hirta* possesses anticandidal activity against *C. albicans* strain in the electron microscopy observations. The *E. hirta* has never been evaluated for anti-*Candida* activity before; it is the first time to study anti-*Candida* activity [18].

Peganum harmala L.

The evaluation of the mixture of natural honey and *P. harmala (pgh)* seeds against *C. albicans* was done to compare the antifungal activity of *pgh* alone and in combination with 6 honeys' from different regions of Algeria against *C. albicans*. The results indicate that the powder of *pgh* and honey are efficient against the tested yeast. The combination of *pgh* with 6 honeys samples were always more efficient. Thus, the mixture of *pgh* and honey could lead to the development of new combination antibiotics against yeast infection. Powder obtained from *pgh* mixed with honey showed a good antifungal action against *C. albicans*. The results showed that adding honey to *pgh* increases the antifungal effect against *C. albicans* [20]. It seems that there is an over-additive action between honey and the tested medicinal plants; this action is also called synergism [21]. The combination of honey plus some natural additives has superior results in its antibacterial, antifungal, and wound-healing promotion properties compared with pure bee honey and some other topical wound agents alone [22].

Allium sativum Linn., *Zingiber officinale* Roscoe.

The in vitro antimicrobial evaluation of lozenges containing extract of garlic and ginger was carried out. Results indicated that there was inhibition of growth by nystatin tablet but garlic and ginger combination only inhibited growth of laboratory strains of *C. albicans*. The results also showed that the garlic and ginger can be

formulated into lozenges and used in non-resistant oral thrush. The garlic and ginger lozenge demonstrated pronounced antifungal activity against the laboratory isolate of *C. albicans* but not against the clinical isolates of the same organism while nystatin gave inhibition zone diameter values of 21 to 41 mm. *Escherichia coli* and *Staphylococcus aureus* strains were resistant [23]. It is however relatively unclear as to why the clinical isolates of *C. albicans* used in the study did not show susceptibility to the garlic and ginger release sample used, given that the antifungal effect of garlic has been previously well established [24, 25, 26, 27, 28,]; especially when this is compared to the results obtained for the standard nystatin tablet where the *C. albicans* strains showed susceptibility. It is worthy to note that in most cases of infection, a combination of antimicrobial activity and one or more other biological effects, such as immunomodulation, could be responsible for overall effect of a natural product [29]. Garlic and ginger have been known to possess immunological and cytoprotective effects in the biological host [30, 28, 31, 32, 33]. It is therefore likely that a combination of these biological effects of garlic and ginger and the demonstrated antimicrobial effect may explain its usefulness in the management of oropharyngeal infections, especially those of fungal origin in folklore medicine [23].

***Ficus lyrata* L.**

The antimicrobial activity of ethyl acetate latex extract of *F. lyrata* and nystatin was carried out on 65 clinical isolates of *C. albicans* from VVC and standard strain of *C. albicans*. The obtained results showed that *F. lyrata* extract has inhibitory effect on clinical isolates and type strain of *C. albicans* in lower concentrations than nystatin drug. The diameter of inhibition zones for nystatin was between 16 to 20 mm and 21 to 24 mm for standard strain and clinical isolates of *C. albicans*. Based on the data analysis, the best MIC of *F. lyrata* ethyl acetate latex extract on clinical isolates and type strain of *C. albicans* were 25 mg/ml and 2.5 mg/ml. The best MIC of nystatin on clinical isolates and type strain of *C. albicans* were 36 mg/ml but MIC of combination of both showed more potency than nystatin alone (0.05mg/ml), which is a synergistic effect [34].

***Oxystelma esculentum* (L.F.) sm.**

O. esculentum is used medicinally in Egypt. Different parts of these plants have been claimed to be effective in a wide spectrum of diseases. The study was based on the effect of herbal medicine or natural products on candidiasis which is a fungal disease caused by the fungi *C. albicans*. The antifungal studies confirmed that the methanol extract of *O. esculentum* (MEOE) had an effective zone of inhibition against *C. albicans* and *Candia neoformans*. The results revealed that MEOE possess zone of inhibition 25 mm against *C. albicans*, and 20 mm against *C. neoformans*. An MIC at 12.5g/ml against *C. albicans* and 50 g/ml against *C. neoformans*, and 500g/ml against other tested fungal organisms were observed. The results were comparable with ketoconozole, which show an MIC at 6.25 g/ml against all tested fungal organisms. In MIC studies, the MEOE had more effect on *C. albicans*, thus giving a lead for further in vivo anticandidal studies [35].

***Sapindus saponaria* L.**

A study of in vivo antifungal activity of the hydroalcoholic extract (HE) and n-BuOH extract (BUTE) of *S. saponaria* against azole-susceptible and resistant human vaginal *Candida* spp. was carried out. The in vitro antifungal activity of HE, BUTE, fluconazole (FLU), and itraconazole (ITRA) was determined by the broth microdilution method and obtained values of MIC and minimum fungicidal concentration (MFC) for 46 strains of *C. albicans* and 10 of *C. glabrata* isolated from patients with VVC. The extracts showed in vitro inhibitory and fungicidal activity against all the isolates, and the MIC and MFC values for the *Candida glabrata* isolates were slightly higher. The results demonstrated that HE and BUTE from *S. saponaria* show inhibitory and fungicidal activity in vitro, in addition to in vivo activity against azole-resistant vaginal isolates of *C. glabrata* and azole-susceptible and resistant isolates of *C. albicans*. With respect to the in vitro susceptibility test for antifungal azoles, a few *C. abicans* were resistant to ITRA, but not to FLU, in concordance with other studies that also recently demonstrated resistance to azoles among vaginal isolates of this yeast [36, 37]. Some isolates of *C. glabrata* were resistant to ITRA and FLU and also to both antifungal simultaneously, also in concordance with studies that demonstrated that vaginal isolates of non-*C. albicans*, principally *C. glabrata*, are less susceptible to azoles than is *C. albicans* [36, 38]. In accordance with the classification of [39] and from the values of MIC50 and MIC90 obtained for the isolates of *C. albicans*, HE and BUTE demonstrated strong inhibitory activity, and moderate to strong activity against *C. glabrata*. The in vitro inhibitory and fungicidal activities of extracts of *S. saponaria* against some vaginal isolates of *C. albicans* and non- *C. albicans* were demonstrated [40]. In the in vivo tests, FLU and HE in a concentration of 5% and BUTE in concentrations of 2.5% and 5% were capable of eliminating the infection induced by the different yeasts tested, including those that were resistant to in vitro tests. These results for in vitro resistant *C. albicans* and principally *C. glabrata* are important because there are few treatment options available for management of patients with VVC caused by these resistant yeasts [36, 37]. It must be considered that *C. glabrata* is the second most frequently isolated species in cases of VVC, preceded only by *C. albicans*; and that in some human populations the rate of isolation of non-*C. albicans* yeasts has increased [41, 42], emphasizing the importance of the antifungal activity of *S. saponaria* and of continuing studies with this plant. The results evidenced the importance of correct identification of the yeasts in cases of VVC, as well as the determination of their in vitro profile of susceptibility to commercially available antifungals, because there were clear differences among the different isolates in the susceptibility profile, both in vitro and in vivo [43].

***Zataria multiflora* Boiss.**

Anti-*Candida* activity of the aqueous, ethanol and methanol maceration extract of the aerial parts of *Z. multiflora* was studied in vitro. Aqueous extract showed no remarkable activity against *Candida* species. Methanol extract of the aerial parts of *Z. multiflora* has more anti-*Candida* effect at 70.7 mg l^{-1} compared to ethanol extract 127 mg l^{-1}. In addition, the isolates of *Candida parapsilosis* were more susceptible to methanol extract than other tested spp. The presence of thymol, rosmarinic acid, and carvacrol in the different parts of the plant was observed [44]. The results indicated that methanol extracts of the aerial parts of *Z. multiflora* have marked activity against isolates of *Candida*. Probably, the anti-*Candida* activity of methanol extract of *Z. multiflora* is due to both rosmarinic acid and thymol that extracted only into methanol [45]. It is concluded that *Z. multiflora* represents an untapped source of potentially useful anti-*Candida* and is worthy for future clinical study [46].

***Zingiber officinale* Roscoe.**

The antifungal efficacy of ethanol extract of ginger on *C. albicans* in vitro was evaluated. The shunti choorna was procured from commercial source. The antifungal activity of the agent was tested in the following dilution range-1g, 2g, 4g of shunti choorna in 99.9% ethanol. Ginger paste at room temperature showed inhibition zone better than ethanol alone, but cold ethanol ginger extract showed the maximum inhibition at 24 hrs. The results indicated that the ethanol extract of ginger powder has pronounced inhibitory activities against *C. abicans*. From the obtained results it was concluded that although ethanol in itself has antifungal activity, ethanol extract of ginger has a synergistic activity [47].

***Combretum zeyheri* Sond.**

C. zeyheri has been reported to exhibit anti-*Candida* activity against *Candida krusei*, *C. albicans*, and *C. parapsilosis*. A bioactivity-guided fractionation of methanol extarct of *C. zeyheri* resulted in the isolation of triterpenoids, ursolic acid (1.1), oleanolic acid (1.2), maslinic acid (2.1), 2a, 3b-dihydroxyurs-12-en-28-oic acid (2.2), 6b-hydroxymaslinic acid (3), and terminolic acid (4). All the isolated compounds, 1.2, 2.1, 2.2, 3, and 4 except ursolic acid (1.1) [48], are being reported for the first time from *C. zeyheri*. Later, the isolated triterpenoids (1–4) were evaluated for their anti-*Candida* activity against the 3 strains of *C. albicans* and all compounds showed anti-*Candida* activity of which terminolic acid (4) was most active. Furthermore, structure–activity relationship of isolated

triterpenoids (1–4) was studied, which showed that triterpenoids of oleanane and ursane having 2a, 3b, 23-trihydroxyl group are more active. It is emphasized that introduction of a-hydroxyl groups at C-2 and C-23 in ursolic acid/oleanolic acid will increase the activity. On the contrary, introduction of a b-hydroxyl group at C-6 position (maslinic acid 3) will decrease the activity. It shows Potential (0.9 lg/ml) anti-*Candida* activity against *C. albicans* for arjunolic acid (6) and asiatic acid (7) [49]. Amphotericin B and clotrimazole were used as controls. It has been first time reported the anti-*Candida* activity for terminolic acid (4). Since terminolic acid (4) is present as a major constituent in ethyl acetate fraction, its structure activity relationship can be studied for optimizing the anti-*Candida* lead. The ethyl acetate fraction of *C. zeyheri* and triterpenoids 1–4 possess anticandidiasis potential and validate the folklore use of *C. zeyheri* for the treatment of infections. These results may be of great help in the development of inexpensive anti-*Candida* drug formulation from a very common and widely distributed plant *C. zeyheri* [50].

***Echinophora Platyloba* DC.**

The effectiveness of the ethanol extract of *E. platyloba* on *C. albicans* was studied. Results showed that the extract of *E. platyloba*, equal or above the concentration of 2mg/ml, effectively inhibits the growth of *C. albicans*. The potential of this extract to inhibit *C. albicans* growth in at least an MIC of 2 mg/ml concentration revealed a reasonable effect against *C. albicans* [51]. The studied plant is one of its 4 species, being endemic of Iran, which grows in many parts of the country [52]. Some steroidal saponin, like CAY-1, has shown to be a potent fungicide against *C. albicans* by disrupting the membrane integrity of the fungal cells, at concentrations below the threshold of mammalian cell toxicity [53, 54]. The study revealed that saponins H1 and H2 had no antimicrobial effect, but saponin Sx1 possessed in vitro antifungal activity with respect to *C. albicans, C. krusei and C. tropicalis* [55]. With the results of the study, it is confirmed that this plant has an effective role in the inhabitation of fungal growth especially against *C. albicans* [51].

***Pogostemon parviflorus* Benth.**

A study was conducted to assay the anti-*Candida* activity of the ethanol extracts and methanol extracts of *P. parviflorus* leaf against opportunistic mycosis causing pathogenic fungi, such as *C. albicans* (5), *C. glabrata* (2), *Candida tropicalis* (2) and *Candida dubliensis* (1), by agar well diffusion method. It was demonstrated that the ethanol extracts and methanol extracts of *P. parviflorus* leaf had inhibitory effects against *Candida* strains. The diameters of growth inhibition zone of the ethanol and methanol extracts were between 8 and 15 mm and 8 and 20 mm. The inhibition zones for Ketoconazole were determined between the 8 and 20 mm. However, the MIC values confirmed the existence of inhibitory effects on *Candida* spp. tested in the study, with MIC values ranging from 2.5 to 20 mg ml−1. The mean of MICs of methanol extracts against 10 isolates of *Candida* was for 5 isolates of *C. albicans* (6.5 mg ml−1), *C. glabrata* (10 mg ml−1), *Candida dubliensis* (5 mg ml-1) and *C. tropicalis* (5 mg ml−1). Likewise, the mean of MICs of ethanol extracts against 10 isolates of *Candida* was for 5 isolates of *C. albicans* (8 mg ml−1), *C. glabrata* (7.5 mg ml−1), *C. dubliensis* (2.5 mg ml−1) and *C. tropicalis* (5 mg ml−1). Thus, it is concluded that the ethanol extract of the tested plant has more anti-*Candida* effect at 5.7 mg ml−1 when compared to the methanol extract at 6.6 mg ml−1. The lowest concentration of the tested plant showed good antifungal activity against *C. dubliensis*, while the highest concentration showed an inhibitory effect against *C. albicans* and *C. glabrata*. Briefly, based on the results, the ethanol extracts and methanol extracts of *P. parviflorus* leaf can be considered as a new source for developing local antifungal agents and as a potent source of natural anti-*Candida* compounds [56].

***Argemone mexicana* Linn.**

The antimicrobial activity of leaf extracts of *A. mexicana* was carried out. In the initial stages the methanol extracts of *A. mexicana* leaf evaluated by antibacterial activity did not show inhibitory action. The results revealed that the extract of *A. mexicana* leaf has a poor antibacterial action. And then this extract evaluated by antifungal activity against human pathogenic yeast strain of *C. albicans, C. tropicalis, Aspergillus niger, Aspergillus flavus, Aspergillus candidus.* The antifungal activity of methanol extracts of *A. mexicana* leaf against fungal strain revealed that these extracts having more potent activity against *C. albicans* as compared to other yeast strain but it is moderate to FLU, and from the MICs of plant leaf extract it was found that the lowest MIC value 3.12mg/ml for methanol extract against the *C. albicans* as compared to other fungal strain [57]. The results obtained revealed that *C. albicans* was the most sensitive with the lowest MIC values of 2.0 mg/ml in the presence of essential oil while *Candida torulopsis* was least sensitive to *A. mexicana* essential oil. The inhibition zone of the essential oil (aerial parts) of *A. mexicana* on *C. albicans* was 11.0 ± 0.2 mm but was resistant to essential oil isolated from the root parts. The inhibition zones recorded for the essential oil of the aerial parts and root parts of *A. mexicana* against *Candida stellatoidea* was almost the same but *C. torulopsis* was resistant to essential oil isolated from the aerial parts and root parts of *A. mexicana*. Except for *C. albicans* in the performance of both the aerial part and root part followed similar pattern. The zones of inhibition were nearly the same. This may probably be due to similar compound being present in both part of the plant at almost similar concentration in the essential oils. The zones of inhibition recorded in the study were lower in size when compared with the results obtained by [58]. The difference could be attributed to the methods used and the compounds on target. Also the variation observed in the study could be due to many factors such as agar composition as well as the volatility of oil in the open air system [59]. The demonstration of sensitivity as a result of incorporation of oil extract of *A. mexicana* at various levels of concentration on *C. albicans*, *C. stellatoidea, C. torulopsis, Klebsiella pnuemoniae, Bacillus subtilis, Staphylococcus aureus* and *Pseudomonas aeruginosa* confirmed the suggestion that the plant oil extract contain potent antimicrobial constituents [60, 61]. The activity shown against *C. albicans, C. stellatoidea* and *C. torulopsis,* further gives credit to the plant, as *Candida* species are known to be resistance to most antibiotic [57].

***Lawsonia inermis* (L) Keay.*, Withania somnifera* L. Dunal**

The bio-activity (antibacterial and antifungal) of ethanol, acetone, Iso propyl alcohol, toluene and hexane extract of different aerial parts (leaf and flower) of *W. somnifera* was evaluated. The extract of *W. somnifera* significantly inhibited 6 important bacteria and two fungi (*C. albicans* and *A. flavus*) to varying degrees. Leaf extracts of *W. somnifera* in different polar solvents showed highest activity in terms of inhibition zone, activity index, MIC, MBC/MFC and total activity. The inhibitory effect is very identical in magnitude and comparable with that of standard antibiotics. Gentamycin, the standard antibacterial drug used was effective in inhibiting these bacteria. The effect on *S. aureus* and *B. subtilis* were comparable to that of gentamycin, ketoconazole, the standard antifungal used was effective against the fungi (*C. albicans* and *A. flavus*) [62].

***Allium sativum* Linn.**

The Anti-*Candida* activity of aqueous extracts of some herbals was studied**.** The inhibition zone diameters by the test isolates against different plant extracts showed that the *Azadirachta indica* and *Murraya koenigii* were showing week and the extract of *A. sativum* bulbs displaying a strong anticandidal activity, against all the species of *Candida* tested. Previous workers have reported that the most effective concentration of the extract of *A. sativum* and the other species of *Allium* against *C. albicans* and Non *C. albicans Candida* species were ranging from 0.5 to 4.0 mg/ml. Based on paired t-test, there is no significant difference between the mean values of the size of zone of inhibition of Amphotericin B and herbal extracts were reported. The extract of *A. sativum* bulbs (1 mg/ml) was reported effective in controlling Candidal growth under in vitro condition [63]. The anti-candidial effect of garlic extract (GE) (*A. sativum*) was studied in normal and streptozotocin induced diabetic rats. Administration of GE significantly reduced *C. albicans* concentrations in liver and kidneys homogenates in infected control and diabetic rats. Treatment of normal and diabetic rats with GE after *Candida* inoculation caused a considerable inhibitory effect on the growth of the organism in both liver and kidneys [64]. Some in-vitro studies confirmed anti-bacterial [65, 66] and anti-Candidal [67, 68] effects of GE but there is a paucity of information regarding the

in-vivo anti-candidiasis efficacy of GE. The results indicate that GE exhibits inhibitory effects against candidiasis in both control and diabetic rats. The anti-candidial effects of garlic attributed mainly to allicin. Allicin, one of the active principles of freshly crushed garlic homogenates, has a variety of anti-bacterial, antifungal (particularly against *C. albicans*), anti-parasitic and anti-viral activities [69]. It has been reported that blockage of lipid synthesis [70], enhancement of phagocytosis and increase in natural killer cell activity [71] may be important components of the anti-candidal activity of garlic. It has been reported that the use of fresh garlic is more effective for antimicrobial activity than that from old garlic [65, 68]. These results indicate that GE exhibits inhibitory effects against candidiasis and therefore validates the traditional use of the plant in fungal infections in diabetic patients. A study on in vitro antimicrobial properties of aqueous GE against multidrug-resistant (MDR) bacteria and *Candida* species from Nigeria reported that the anticandidal effect of aqueous garlic extract (AGE) resulted in a growth inhibition zone of 27.4 ± 3.7 mm with no significant difference ($P > .05$) in MIC values at 24 and 48 hours. MFC were found to be 14.9 and 15.5 mg/mL, at these incubation periods. The observed zone of inhibition on agar of gram-positive and gram-negative bacteria and *Candida* isolates were comparable to those elicited by ciprofloxacin and FLU, showing that the isolates exhibited susceptibility. This indicates that AGE has a broad spectrum of antimicrobial activity and a wide therapeutic window [72].

***Foeniculum vulgare* Miller., *Trachyspermum ammi* Linn., *Syzygium aromaticum* Linn., *Cuminum cyminum* Linn., and *Cinnamomum tamala* Linn.**

Taking into account, 5 different plants viz., *F. vulgare*, *T. ammi*, *C. cyminum*, *S. aromaticum* and *C. tamala* were selected for anti-candidal activity against *Candida* species (*C. albicans, C. glabrata, Candida heamolonii*). All the plant extracts showed antimicrobial activity against at least 3 of the *Candida* strains tested, as exhibited by an antimicrobial screening assay. Extracts of *F. vulgare, T. ammi, C. cyminum, S. aromaticum*, *C. tamala* showed the most potent activity against the entire microorganism studied *C. albicans, C. glabrata*, *C. haemolonii*. The acetone, methanol, benzene, ethyl acetate and chloroform fraction of leaves were evaluated, the antifungal activity was more effective in acetone and methanol extracts of *C. tamala* against *Candida* species. The *Candida* growth inhibition of various solvent extract was found in the range from 94-98 mm against *C. albicans, C. glabrata* and *C. heamoloni*. On the contrary, *C. albicans, C. glabrata* and *C. haemolonii* strains were found to be more sensitive to extracts of *C. tamala, C. tamala. C. tamala* showed good anti-*Candida* activity against MDR strains of *C. albicans, C. glabrata, C. heamolonii*. Whereas the zones of inhibition for ITRA, clotrimazole, ketoconazole and nystatin against *C. albicans* were (24, 20, 29 and 14 mm), against *C. glabrata* (19, 31, 29 and 19mm) and against *C. heamolonii* (20, 30, 37 and 19mm). The MIC of the extract of *C. tamala* was found 6.25 X 10^{-4} against *C. albicans* and *C. glabrata* while *C. heamolonii* was found to be 12.5 X 10^{-3}. The extract of *C. tamala* showed fungicidal effect against the pathogen tested. The MFC of the extract against *C. albicans* and *C. glabrata* showed 6.25 X 10^{-4}, while MFC of the *C. heamolonii* was found 12.5 X 10^{-3}. The extract of *C. tamala* showed a broad spectrum antifungal activity against *Candida* strains. The results showed inhibition at concentrations as low as 6.25 X 10^{-4} (*C. tamala*). The variation of susceptibility of the tested microorganisms could be attributed to their intrinsic properties that are related to the permeability of their cell surface to the extracts. Due to the emergence of antibiotic resistant pathogens in hospitals and homes, plants are being looked upon as an excellent alternate to combat the further spread of MDR microorganisms. The 2 solvents (acetone and methanol) based extracts of *C. tamala* showed good activity but the acetone extract was highly active against *Candida* strains. The results also showed that the methanol extract (*C. tamala*) is highly active against *C. glabrata* and *C. heamolonii*. It is interesting to note that even crude extracts of these plants showed good activity against MDR strains where modern antibiotic therapy has failed. The extract of *C. tamala* could be a possible source to obtain new and effective herbal medicines to treat infections caused by MDR strains of microorganisms. The results noticed in the study showed that the extracts obtained from the selected medicinal plants collected from Meerut region had anti-*Candida* activity and can be used in preparation of novel natural therapeutic drugs against *Candida* associated infections [73].

***Cinnamomum cassia* (Nees) Nees ex. Blume.**

An attempt was made to determine the phytochemical composition and in vitro effects of methanol extract of *C. cassia* bark against *C. parapsilosis*, *Candida guilliermondii* and *C. glabrata*. The crude methanol extract was found to have MIC of 800, 800 and 1600µg/ml against *C. parapsilosis*, *C. guilliermondii* and *C. glabrata*. The results revealed that the test extract (TE) showed more killing in case of *C. parapsilosis* and *C. guilliermondii*. It would appear that *C. glabrata* is the less sensitive yeast to the TE. The results obtained provided obvious evidence that the TE used in the study has a substantial level of antifungal activity. SEM examination of treated cells showed severe damage of the membrane. Antifungal activity (in vitro) of the TE was studied against 3 *Candida* isolates at 3 different concentrations (4, 8 and 12mg/ml). At 4mg/ml the activity shown was very less. The degree of inhibition varied with the concentration of the TE. The highest zone of inhibition i.e. 11 mm was measured in *C. guilliermondii* when treated against 12mg/ml of the TE, followed by 10 mm measured in *C. parapsilosis* when treated with the same concentration of the TE. In case of *C. glabrata* at highest concentration of the TE the zone of inhibition was only 8mm. In comparison FLU at 100µg/ml showed 17, 15 and 15 mm, zone of inhibition in *C. parapsilosis*, *C. guilliermondii* and *C. glabrata*. The results show that, in case of control disc no zone of inhibition was observed so as far as the study is concerned 1% DMSO, as a solvent is having no effect on the tested organisms. Hence it is effectively concluded that whole of the antifungal effect is due to the different concentration of the TE. The findings by SEM suggest that this potential bioactive extract has distinct influence on *Candida* cell by causing breakage in the cell membrane and leakage of cellular content. The TE shows significant anti-*Candida* activity both in liquid and solid medium. From the data, it is concluded that *C. cassia* bark extract can be explored further as an option for efficacious and safe drug for candidiasis [74].

***Hybanthus enneaspermus* F Muell.**

The investigation was carried out to evaluate the antifungal efficacy of the different plant extracts of *H. enneaspermus*. The antifungal property of the petroleum ether, chloroform and methanol extracts of the plant *H. enneaspermus*, were tested against a group of fungi, viz., Aflatoxin producing fungi, *A. flavus*, *Aspergillus fumigatus* and human pathogenic fungi *C. albicans* and *C. tropicalis* by well diffusion method. The methanol extract exhibited significant antifungal activity on most of the fungal strains, viz. *A. flavus, A. fumigatus, C. albicans* and *C. tropicalis* followed by the petroleum ether extract and chloroform extract. The results indicated that as the concentration of the plant extract increased, the zone of inhibition produced also found to be increased. All the extracts showed high to moderate zone of inhibition against 4 fungal strains when compared to the standard drug FLU [75].

Table 1: In vitro studies considering the plants with beneficial effects on vaginitis

Effect	Method	Part of plant ± active compound	Family	Plant	Ref.
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Euphorbiaceae	*Acalypha indica* L.	[67]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of clove	Liliaceae	*Allium sativum* L.	[67]

Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of clove	Liliaceae	*Allium schoenoprasum* L.	[67]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of bulb	Liliaceae	*Allium cepa* Var. aggregatum L.	[67]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of bulb	Liliaceae Cepa L.	*Allium cepa* Var.	[67]
Anti-*Candida* activity	Media culture	Essential oil	Verbenaceae	*Aloysia triphylla*	[39]
Anti-*Candida* activity	Media culture	Essential oil	Compositae (Asteraceae)	*Anthemis nobilis*	[76]
Anti-*Candida* and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Apiaceae (Umbelliferae)	*Anethum graveolens*	[76]
Anti-*Candida* and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Compositae	*Artemisia sieberi*	[76]
Anti-*Candida* and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Compositae	*Artemisia dracunculus*	[76]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf and seed	Meliaceae	*Azadirachta indica* A. Juss	[67]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Theaceae	*Camellia sinensis* (L.) O. Ktze	[67]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of fruit (dry and green)	Solanaceae	*Capsicum annum* L.	[67]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Caesalpiniaceae	*Cassia alata* L.	[67]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Caesalpiniaceae	*Cassia fistula* L.	[67]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Caesalpiniaceae	*Cassia occidentalis* L.	[67]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of seed	Rubiaceae	*Coffia Arabica* L.	[67]
Anti-*Candida* and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Rutaceae	*Citrus aurantifolia*	[76]
Anti-*Candida* and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	-	*Communis hominis*	[76]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extract of rhizome	Zingiberaceae	*Curcuma longa* L.	[67]
Anti-*Candida* activity	Media culture	Essential oil	Poaceae	*Cymbopogon martini*	[39]
Anti-*Candida* activity	Media culture	Essential oil	Poaceae	*Cymbopogon winterianus*	[39]
Anti-*Candida* activity	Media culture	Essential oil		*Cyperus articulates*	[39]
Anti-*Candida* and ant-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Myrtaceae	*Eucalyptus globulues*	[76]
Anti-*Candida* and ant-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Apiaceae	*Foeniculum vulgare*	[76]
Anti-*Candida* activity	Media culture	Extracts of flowers and leaves	Asteraceae	*Inula viscose*	[77]
Fungistatic and fungicidal activity against *C. albicans* strains	Media culture	Essential oil	Lamiaceae	*Lavandula anguistifolia*	[78]
Anti-*Candida* and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Lamiaceae	*Lavandula estoechas*	[76]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Lythraceae	*Lawsonia inermis* L.	[67]
Anti-*Candida* activity	Media culture	Essential oil		*Lippia alba*	[39]
Anti-*Candida* activity	Modification of the CLSI (formerly NCCLS) reference M27-A2 broth-micro dilution	Essential oil	Myrtaceae	*Melaleuca alternifolia* Cheel.	[79]
Anti-*Candida* activity	Media culture	Essential oil	Lamiaceae	*Mentha arvensis*	[39]
Anti-*Candida* activity	Media culture	Essential oil	Lamiaceae	*Mentha piperita*	[39]
Anti-*Candida* activity	Media culture	Essential oil	Lamiaceae	*Mentha sp.*	[39]
Anti-*Candida* and anti-activities	Punched-Whole Test and Paper-bacterial Disc Test	Essential oil	Lamiaceae	*Mentha spicata*	[76]
Anti-*Candida* activity	Media culture	Essential oil	Asteraceae	*Mikania glomerata*	[39]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of leaf	Labiateae	*Ocimum sanctum* L.	[67]
Anti-*Candida* activity	Media culture	Essential oil	Lamiaceae	*Origanum vulgare* L.	[67]
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol	Piperaceae extracts of leaf	*Piper betel.* L.	[67]
Inhibited Mycelia growth of *C. albicans*	Colorimetric assay	Bourbon geranium oil	Geraniaceae	*Pelargonium asperum*	[80]
Anti-*Candida* and anti-	Punched-Whole Test and Paper-	Essential oil	Geraniaceae	*Pelargonium roseum*	[76]

bacterial activities	Disc Test				
Anti-*Candida* activity	Two-fold serial dilution technique	Water and ethanol extracts of seed	Papilionaceae	*Psoralea corylifolia.* L.	[67]
Anti-*Candida* and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Lamiaceae	*Rosmarinus officinalis*	[76]
Anti-*Candida* activity	Broth micro- dilution assay	Extracts of dried fruits and saponin	Sapindaceae	*Sapindus saponaria* L.	[40]
Anti-*Candida* activity	Media culture	Essential oil	Lamiaceae	*Satureja montana* L.	[81]
Anti-*Candida* and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Lamiaceae	*Saturella hortensis*	[76]
Anti-*Candida* activity	Media culture	Essential oil	Asteraceae	*Solidago chilensis*	[39]
Anti-*Candida* activity	Media culture	Essential oil	Lamiaceae	*Stachys byzantine*	[39]
Anti-*Candida* activity	Microbroth dilution assay	Steroid saponins	Zygophyllaceae	*Tribulus terrestris* L.	[82]
Anti-*Candida* activity	Agar well diffusion assay	Ethanol extracts of the rhizomes and Above ground portion	Liliaceae	*Trillium grandiflorus* (Michx.) Salibs	[83]
Anti-*Candida* activity	Media culture	Essential oils	Lamiaceae	*Thymus vulgaris*	[81]
Anti-*Candida* and anti-bacterial activities	Punched-Whole Test and Paper-Disc Test	Essential oil	Lamiaceae	*Zataria multiflora*	[76]
Anti-*Candida* activity	Broth micro-dilution assay	Extract medium	Poaceae	*Zea mays*	[84]

CONCLUSION

Nowadays, the indiscriminate use of commercial antimicrobial drugs has caused multiple drug resistance in human pathogenic microorganisms. The resistance strains of *C. albicans* have become a cause of major health concerns and require novel antifungal agents to tackle this problem. This situation forced scientist to search for new and effective antimicrobial agents to replace the current regimens. Plants have been a key source for the discovery of new drugs and higher plants may provide a potential antifungal lead against the resistance strains of *C. albicans*.

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