www.bti.org.in
ISSN 0974-1453
Review article

AN EMERGING HOPE TO COMBAT *CANDIDA ALBICANS*: PLANT BASED THERAPEUTICS

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ABSTRACT: *Candida* associated morbidity and mortality is reported to increase at an alarming rate worldwide due to its lead role in hospital acquired infections (Nosocomial infections). Rising incidences on resistance in *Candida* species to existing antifungal drugs and the frequent occurrence of Candidosis have prompted the researchers to look for alternative therapeutics. Several plant extracts have been screened by various groups for anti-Candidal properties. These plants could provide cost effective and safer approach of treating Candidosis, justifying the basis for developing herbal drugs against the deadly pathogen. In this review we have compiled more than hundred studies demonstrating the ability of plant extracts to combat *Candida* pathogenesis, with a perspective of developing herbal anti-*Candida* drugs.

Keywords: Anti-*Candida* Plants, Plant Extracts, Candidosis, Herbal drugs, *Candida* pathogenesis, Alternative drugs.

INTRODUCTION

Classification of C*andida:*

Kingdom: Fungi

Phylum: Ascomycota

Subphylum: Saccharomycotina

Class: Saccharomycetes

Order: Saccharomycetales

Family: Saccharomycetaceae

Genus: *Candida*

Candida is ubiquitous, dimorphic, opportunistic fungus that affects humans. It remains in commensal association with many animals. The infection of candida primarily depends upon the immune status of the host. *Candida* is usually diploid and naturally heterozygous yeast. *Candida albicans* displays three modes of growth: yeast, hyphae and pseudohyphae (Fig. 1), which are inter-convertible depending upon the environmental conditions. These all three differ in their morphology and pathogenicity. Of all three morphology, hyphal and pseudohyphal are pathogenic.

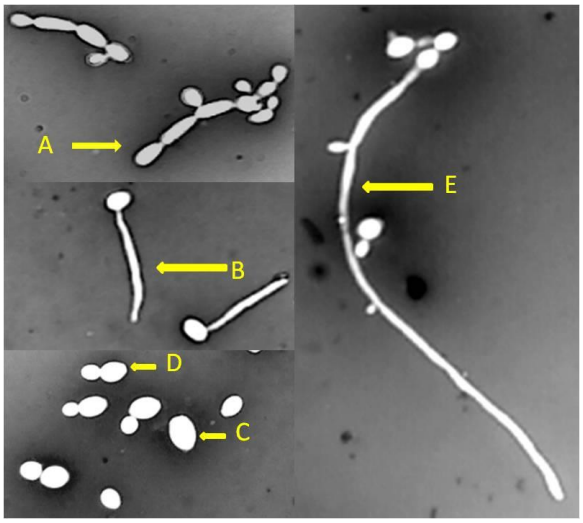

FIGURE 1: Different morphological forms of *Candida* species at 100X resolution. A- Pseudohyphae, B- Germ Tube, C- Yeast form, D- Budding form, E- Hyphae. Hyphae and pseudohyphae are induced using 10% Serum.

Now about 200 *Candida* species are known to us and of which only few are involved in human infection. More than 90% of Candidemia is caused by five *Candida* species: - *C. albicans, C. glabrata, C. tropicalis, C. krusei* and *C. parapsilosis* (Hajjeh *et al*., 2004; Takakura *et al*., 2004; Arendrup *et al*., 2005). Candidemia may also be caused by several other non *albican*s *Candida* species like *C. dubliniensis, C. famata, C. guilliermondii, C. lusitaniae, C. norvegnesis,*

C. pelliculosa and C. rugosa (Takakura *et al*., 2004; Sandven *et al*., 2008). Although these species are unusual cause of Candidiasis, but some of them are found to be associated in nosocomial clusters, or even obtained resistance to antifungal drugs (Colombo *et al*., 2003; Colombo *et al*., 2006).

Candida is the benign species of yeast micro-flora that initially causes a superficial mucosal infection and then with time moves deeper into bloodstreams, result into systemic infection. In its hyphal form mainly, it invades the epithelial tissue and penetrates deeper into tissues. After *C. albicans, C. glabrata* is the second or third most cause of Candidiasis and is not dimorphic in nature.

Based on the part of the body where infection has occurred, the main types of *Candida* infections are systemic Candidiasis, oral thrush, oesophageal thrush, cutaneous Candidiasis, Candida vaginitis and Candida balanitis. Blood stream infection of *Candida* is called Candidemia that is the most frequent clinical manifestation and causes significant morbidity and mortality in hospitalized patients.

Candida species is the fourth most frequent cause for nosocomial systemic infection in ICU patients. Also, this yeast is the third most widespread cause of nosocomial bloodstream infections (Alimirante *et al*., 2005). Various factors contribute towards such a high rate of this infection like lack of resource for medical care and training programs, difficulties in controlling the infection in hospitals in developing countries, shortage of staff in healthcare and less effective anti-fungal drugs. Mostly cases of *Candida* infection reported include areas of neonatal, paediatric and adult-ICUs because these persons have suppressed immune responses against *Candida*. The three major groups of patients that are at high risk of Candidiasis are with neutropenic cancer, organ or stem cell transplant and those undergoing intensive care procedures. In past few years, it has been observed that the patients having a central venous catheter, receiving parental nutrition or on broad-spectrum

antibiotics are also at high risk. They have high acute physiology and chronic health evaluation scores (Rangel-Frausto *et al*., 1999; Michalpopulos *et al*., 2003; Pappas *et al*., 2003). It causes severe infection ranging from superficial muco-cutaneous to tissue invasive. A limited number of drugs are available against it. This problem is contributed due to the factors like dimorphic transition, adhesion, invasion, resistance to phagocytosis and ability to grow well at 37^{o}C. Of many species, *Candida albicans* receive special attention because of its association with humans.

The exact mechanism involved in candidiasis is not known but it is clear that there must be some imbalance occurs between host-pathogen relationships that must be in favour of pathogen (Chakravarthi *et al*., 2010). According to geographical settings and demographics of the population studied, the frequency of systemic Candidiasis varies in blood samples. Due to the large use of fluconazole drugs for the treatment of HIV-infected patients having candidiasis results in the less drug resistant strains of the yeast in early 1990s. These resistant strains emerged out because of their acquisition with previously sensitive *C. albicans* (Sanglard *et al*., 2002). But according to the information gathered from Population-based and sentinel surveillance programs worldwide, it was observed that frequency of fluconazole resistance among *C. albicans* remains insignificant (Hajjeh *et al*., 2004; Alimirante *et al*., 2005; Colombo *et al*., 2006).

Another new thing was noted in numerous hospitals that the frequency of *C. glabrata* is enhanced as a serious *Candida* infection (Baddley *et al*., 2001; Malani *et al*., 2001). Reasons for this include living habitat, age and type of the patients and use of fluconazole. Also *C. glabrata* infection is mainly noted in persons more than 60 years (Malani *et al*., 2001) and in those who have leukaemia or received stem cell transplant and those who are associated with increasing use of fluconazole (Marr *et al*., 2000).

CURRENT STATUS OF CANDIDOSIS

Candida infections are increasing alarmingly in India. According to a report, the most common are *C. albicans* (47%) followed by *C. Tropicalis* (23%). In one of the study at a multi super-speciality centre in southern India, it is found that 74% of incidences of Candidaemia have been due to non-*albicans Candida*. Of which *C. tropicalis* accounted for 39.7% of cases, followed by *C. albicans* (26.4%), *C. lipolytica* (5.8%), *C. famata* (4.4%), *C. parapsilosis* (4.4%), *C. pelliculosa* (4.4%), *C. Guilliermondii* (2.9%), *C. Lusitaniae* (1.4%), *C. sphaeria* (1.4%) and other *Candida* species (8.8%). A study done in the Tertiary Care Institute in India (BL Kapur Memorial Hospital, Delhi) suggested that 18% of all nosocomial blood infection is caused by *Candida* species and reported 53 incidence of Candidaemia in 48 patients in 17 months. They found that 45% of incidences were due to *C. tropicalis,* 23% by *C. albicans* and 32% by other Candida species. The study of susceptibility profile of *Candida* isolates showed 100% sensitivity to voricinazole, 92% to amphotericin B, 90% to flucytosine and 75% to fluconazole. But a study from India suggested that candida isolates has shown a very high resistance to voriconazole (56%), fluconazole (36%), itraconazole (24%), but shown susceptibility of 92% to amphotericin B and 96% to flucytosine. While according to a report from western India, *C. albicans* is associated with 50-70% of all cases of Candidaemia (Report by A. Kothari and V. Sagar, 2009 and Brief communication by R. Adhikary and S. Joshi, 2011).

In US, Candidemia infection is the fourth most widely hospital acquired infection (HAI) (Wisplinghoff *et al*., 2004). According to a report (Hajjeh *et al*., 2004), frequency of Candidal HAI in US is 1.5 cases per 10,000 patients days, whereas in Europe, frequency is slightly lower to 0.5-0.7 cases per 10,000 patients days (Richet *et al.* ,2002; Marchetti *et al.*,2004). In 2006, the highest cases of Candidemia infection reported from Brazil, i.e,

3.7 cases per 10,000 patients days (Colombo *et al., 2006*).

In US, from 1997 to 2001 mortality rate was about 49% for Candidemia patients in medical centres (Gudlaugsson *et al.,* 2003) that was higher than earlier by 11% from 1983 to 1988 (Wey *et al.,* 1988). According to some of the analysis, incidences of Candidemia get complicated with time. The major cases of Candidemia results from *Candida albicans* that mainly causes infection in immune-competant patients. This rate, in Netherland, rose from 0.37 to 0.72 cases per 10,000 patients days between 1987 to 1995 (Voss *et al.,* 1996). While in Switzerland, the rate remains same approximately between 0.5 cases per 10,000 patient day from 1991 to 2000 (Fidel, 2006).

Various factors contribute towards such a high rate of this infection like lack of resource for medical care and training programs, difficulties in controlling the infection in hospitals in developing countries, shortage of staff in healthcare and less effective anti-fungal drugs.

POSSIBILITIES WITH PLANT BASED THERAPEUTICS

From the time immemorial, the plants are serving humans in several ways. The use of plant resources for medicinal and other purposes is one of a number of practices developed by ancient people. Most of the world's population relies on herbal medicine (Lewington *et al*., 2003). In ancient times, plants used randomly without knowing the exact compound that are responsible for its therapeutic responses. But nowadays, as the advances going in herbal medicines, the active chemical in plants are now known to us and their efficacy is also known. In most developing countries, the indigenous modes of herbal treatment are a part of the culture and the dominant method of healing therapy. Reviews have compiled modern researches, which have proven the ability of plant extracts against different pathophysiological conditions and pathogenic infections (Nagle and Zohu, 2006; Anand *et al*., 2012; Rai *et al*., 2012; Joshi *et al*.,

2013; Ruwali *et al*., 2013; Kumar *et al*., 2013). These remedies, with a considerable extent of effectiveness, are socially accepted, economically viable and, mostly, are the only available source. WHO has listed 20,000 medicinal plants used in different parts of the world. Other estimates indicate the number to range between 35,000 and 70,000 worldwide (Lewington *et al*., 2003; Bhattarai *et al*., 2004). Several medicinal systems of the world are dependent upon plants like- Chinese, Tibetan, Indian (Ayurveda), Unani, Siddha and Homeopathy systems. Many countries, especially in Asia, Africa and East European countries, have officially recognized the use of plant-based traditional medicine in their health care delivery systems. WHO has estimated that 80% of the world's populations rely primarily on traditional medicine (WHO Technical Report Series, No. 622:8, Geneva, Switzerland; Okerele, 1992). Considering the coverage and effectiveness of various systems of traditional medicine throughout the world, the Alma-Ata Declaration of the WHO in 1978 proposed the theme "**Health for all by the year 2000**".

These plants provide a way for treating those pathogenic diseases against which no drug is available or for which pathogens are becoming resistant. In the present article, we are providing the information about more than 100 plants and their different extracts, showing anti-*Candida* properties (specifically against *C. albicans*) that have been screened till now, all over the globe.

Table 1: PLANTS SHOWING ANTI-*CANDIDA* PROPERTIES ALONG WITH THEIR PHYTOCONSTITUENTS AND OTHER RELATED PARAMETERS AND SOURCE REFERENCES.

Sr. No.	**Plant (Family) [Reference]**	**Plant Part**	**Extraction Solvent**	**Phytochemical constituents**	**ZOI (mm)**	**MIC_{50} µg/ml**	**MFC_{50} µg/ml**
1	*Aloe vera* (Xanthorrhoeaceae) [Yebpella *et al*., 2011;	Leaf pulp,	Methanol	(Anthraquinones/ anthrones, carbohydrates, chromes, inorganic &	18-25	NI	NI

	Hamman *et al*., 2008*; Ibrahim *et al*., 2011]	Green grid	Ethanol Acetone	organic compound, amino acids, vitamins and saccharides.)* Flavonoids, tannins, steroid	9.96 10.20	NI NI	NI NI
2	*Sapindus saponaria* (Sapindaceae) [Damke *et al*., 2011; Tzuzuki *et al*., 2007*]	Fruit pericarp	Hydroalcohol butanol	(Triterpene saponin-S1, S2 & oligoglycoside-1(OGSA-1))*	NI NI	9 36	310 150
3	*Punica granatum* (Lythraceae) [Endo *et al*., 2010; Hoffling *et al*., 2010; Pai *et al*., 2010; Beckman, 2007*]	Fruit peel Fruit Fruit	Hydro-alcoholic Dichloro-methane Methanol Aqueous	Punicalagin NI NI (Tannins)*	NI NI NI 22-18.8	3.9 1 3 NI	NI NI NI NI
4	*Acacia nilotica* (Fabaceae) [Khan *et al*., 2009; Pai *et al*., 2010]	Bark Leaves	Aqueous Ethanol	Tannins NI	4.62-7.62 26-35	NI 4.9	NI 19.5
5	*Cuminum cyminum* (Apiaceae) [Khan *et al*., 2009]	Dried seeds	Diethyl ether	Oil	1.81-6.5	NI	NI
6	*Cinnamomum vernum* (Lauraceae) [Ababutain *et al*., 2011; Bakkali *et al*., 2005*; Redding *et al*., 1993*; Saad *et al*., 2005*]	Bark	ethanol	[Phenol (eugenol), tannins, flavonoids]*	3.8	25	-
7	*Syzygium aromaticum* (Myrtaceae) [Ababutain *et al.,* 2011; Bakkali *et al*., 2005*; Redding *et al*., 1993*; Saad *et al*., 2005*; Khan *et al*., 2009; Hammer *et al*., 1999]	Buds Buds Bud	Ethanol Ethanol AC	Phenol (Eugenol)* Aldehyde (Cinnamaldehyde) Essential oil	4.8 >40 NI	12.5 156 0.12	NI 156 NI
8	*Vitex negundo* (Verbenaceae) [Kumar *et al*., 2011]	Leaf	Aqueous Ethanol Methanol	NI NI NI	6-5 3 2.5-0.5	NI NI NI	NI NI NI
9	*Adathoda vasica* (Acanthaceae) [Kumar *et al*., 2011]	Leaf	Aqueous Ethanol Methanol	NI NI NI	7-4 5-3 2-1	NI NI NI	NI NI NI

10	*Azadirachta indica* (Meliaceae) [Kumar *et al.*, 2011; Panda *et al*., 2012]	Leaf	Aqueous Ethanol Methanol Benzene	NI NI NI	3.5-2 2 3-1	NI NI NI	NI NI NI
		Leaves	Chloroform Ethanol	NI NI NI	13 16 10	26.3 13.15 52.6	NI NI NI
11	*Mentha piperita* (Lamiaceae) [Kumar *et al*., 2011; Hammer *et al*., 1999; Sartoratto *et al*., 2004]	Leaf	Aqueous Ethanol Methanol	NI NI NI	4-3 2-1 2-1.5	NI NI NI	NI NI NI
		Herb	AC	Essential oil	NI	0.5	NI
		Aerial part	AC	Essential oil 3-octanol, isopentyl-n-butyrate, linalool, *cis-p*-menth-2-en-1-ol, terpin-4-ol, α-terpineol, carvone, β-bourbonene, *trans*-caryophillene, germacrene D,	NI	0.74	NI
12	*Curcuma longa* (Zingiberaceae) [Kumar *et al*., 2011]	rhizome	Aqueous Ethanol Methanol	NI NI NI	2.5 3.5-1 5-3	NI NI NI	NI NI NI
13	*Matricaria chamomillathyme* (Asteraceae) [Dalirsani *et al*., 2011]	Herb	Methanolic	NI	18.98	NI	NI
14	*Allium vineale* (Amaryllidaceae) [Dalirsani *et al*., 2011; Xia *et al*., 2005*; Ankri *et al*., 1999*; Wang *et al*., 2000*; Wang *et al*., 2001*]		Methanolic	(Alliumin, allicin, allivin, lillin)*	18.64	NI	NI
15	*Cinnamomum zeylanicum* (Lauraceae) [Dalirsani *et al*., 2011; Singh *et al.*, 1995*; Khan *et al*., 2009]	Bark	Methanolic Ethanol	(Cinnamic aldehyde)* NI	14.92 >40	NI 19.5	NI 78
16	*Eugenia aromatic* (Myrtaceae) [Dalirsani *et al*., 2011]		Methanolic	NI	15.26	NI	NI

17	*Salvia officinalis* (Lamiaceae) [Dalirsani *et al*., 2011; Hammer *et al*., 1999]	Herb	Methanolic AC	NI Essential oil	14.8 NI	NI 0.5	NI NI
18	*Thymus serpyllum* (Lamiaceae) [Dalirsani *et al*., 2011]		Methanolic	NI	8.81	NI	NI
19	*Momordica charantia* (Cucurbitaceae) [Mwambete *et al*., 2009]	Fruit	Methanol Petroleum ether	Momordin, α- & β-momocharin, cucurbitacin B1 and oleanolic acid	10 8	NI	NI
20	*Cassia occidentalis* (Fabaceae) [Arya *et al*., 2010]	Leaf	Methanol aqueous	NI NI	8 5	NI NI	NI NI
21	*Berchemia discolour* (Rhamnaceae) [Samei *et al*., 2010]	Leaves Bark	Hexane Acetone Hexane Acetone	 NI	12-10 - - -	3.75 0.23 7.5 3.75	7.5 - 7.5 -
22	*Cassine transvaalensis* (Celastraceae) [Samei *et al*., 2010]	Bark	Hexane	NI	16-12	0.46	3.75
23	*Diospyros mespiliformis* (Ebenaceae) [Samei *et al*., 2010]	Leaves	Hexane	NI	7	-	-
24	*Piper capense* **(**Piperaceae**)** [Samei *et al*., 2010]	Root	Acetone Hexane	NI	24-22 12-8	1.88 3.75	3.75 7.5
25	*Warburgia salutaris* (Canellaceae) [Samei *et al*., 2010]	Bark Leaves	Acetone Hexane Acetone Hexane	 NI	22-7 16-10 15 22-16	3.75 0.23 7.5 7.5	7.5 0.93 0.0 -
26	*Anethum graveolens* (Apiaceae) [Zeng *et al*., 2011]	Leaves	Aqueous (Steam)	Essential oil (Carvone and limonene)	NI	0.625	NI
27	*Foeniculum vulgare* (Apiaceae) [Pai *et al*., 2010]	Seeds	Diethyl-ether	NI	2.5	NI	NI
28	*Pisidium guajava* (Myrtaceae) [Jebashree *et al*., 2011; Suvarna *et al*., 2009]	Leaves	Hexane Ethyl acetate Ethanol Methanol Aqueous Methanol	 NI NI	16 16 15 15 11.3 11.7	NI NI NI	NI NI NI

			Chloroform Petroleum-ether		12.7 10.3	NI	NI
29	*Terminalia chebula* (Combretaceae) [Jebashree *et al*., 2011]	Dried fruits	Hexane Ethyl acetate Methanol	NI	12 16 11	NI NI NI	NI NI NI
30	*Achyranthes aspera* (Amaranthaceae) [Jebashree *et al*., 2011]	Stem	Ethyl acetate Ethanol Methanol	NI	15 12 13	NI NI NI	NI NI NI
31	*Rosmarinus officinalis* (Lamiaceae) [Hoffling *et al*., 2010; Hammer *et al*., 1999]	Leaves Herb	Dichloro-methane Methanol Essential oil	NI NI NI	NI NI NI	7 1 1	NI NI NI
32	*Arrabidaea chica* (Bignoniaceae) [Hoffling *et al*., 2010]	Leaves	Dichloro-methane Methanol	NI NI	NI NI	15 7	NI NI
33	*Tabebuia avellanedae* (Bignoniaceae) [Hoffling *et al.*, 2010]	Bark	Dichloro-methane Methanol	NI NI	NI NI	Resistant 3	NI NI
34	*Syzygium cumini* (Myrtaceae) [Hoffling *et al*., 2010]	Seeds	Dichloro-methane Methanol	NI NI	NI NI	30 1	NI NI
35	*Cassia tora* (Caesalpinaceae) [Panda *et al*., 2012; Maji *et al*., 2010]	Leaves	Benzene Chloroform Ethanol Water Acetone Benzene	NI NI NI NI NI NI	10 10 16 4 6 5	26.3 13.15 26.3 - - -	NI NI NI - - -
36	*Lawsonia inermis* (Lythraceae) [Panda *et al*., 2012]	Leaves	Benzene Chloroform Ethanol	NI NI NI	7 7 11	26.3 13.15 52.6	NI NI NI
37	*Pseudolachnostylis maprouneifolia* (Phyllanthaceae) [Panda *et al*., 2012]	Leaves	Hexane Acetone	NI	10-0 0.0	>7.5 1.88	7.5 0.0
38	*Lipia javanica* (Verbenaceae) [Panda *et al*., 2012]	Leaves	Hexane Acetone	NI	10-0 -	3.75 >7.5	- -

39	*Maeruae dulis* (Capparaceae) [Panda *et al*., 2012]	Root	Hexane Acetone	NI	- -	3.75 1.88	- -
40	*Bauhinia galpinii* (Fabaceae) [Panda *et al*., 2012]	Bark Leaves	Hexane Hexane Acetone	NI NI NI	- - -	1.88 1.88 0.23	- - -
41	*Bridelia micrantha* (Phyllanthaceae) [Panda *et al*., 2012]	Bark	Acetone Hexane	NI NI	- -	>7.5 3.75	- -
42	*Bridelia mollis* (Euphorbiaceae) [Panda *et al*., 2012]	Leaves	Acetone Hexane	NI NI	- -	3.75 >7.5	- -
43	*Cassia petersiana* (Fabaceae) [Panda *et al*., 2012]	Bark	Acetone	NI	-	>7.5	-
44	*Capparis tomentosa* (Capparaceae) [Panda *et al*., 2012]	Root	Acetone	NI	-	3.75	-
45	*Pouzolzia mixtra* (Urticaceae) [Panda *et al.*, 2012]	Leaves	Acetone Hexane	NI	-	>7.5 3.75	-
46	*Rhoicissus tridentate* (Vitaceae) [Panda *et al*., 2012]	Tubes	Acetone Hexane	NI	-	>7.5 3.75	-
47	*Schotia barchypet ala* (Fabaceae) [Panda *et al*., 2012]	Bark	Hexane	NI	-	3.75	-
48	*Strychnos decussate* (Loganiaceae) [Panda *et al*., 2012]	Bark	Acetone Hexane	NI	-	3.75 3.75	-
49	*Senna didymobotrya* (Fabaceae) [Panda *et al.*, 2012]	Root	Acetone Hexane	NI	-	7.5 7.5	-
50	*Terminalia sericea* (Combretaceae) [Panda *et al*., 2012]	Root	Acetone	NI	-	1.88	-
51	*Mangifera indica* (Anacardiaceae) [Suvarna *et al.,* 2009]	Leaves	Aqueous Methanol Chloroform Petroleum-ether	NI NI NI NI	7.7 10.7 6.3 5.7	NI NI NI NI	NI NI NI NI
52	*Ixora parviflora* (Rubiaceae) [Suvarna *et al.,* 2009]	Leaves	Aqueous Methanol Chloroform Petroleum-	NI NI NI	11.3 10.7 9	NI NI NI	NI NI NI

			ether NI		13	NI	NI
53	*Calotropis procera* (Asclepiadaceae) [Suvarna *et al*., 2009]	Leaves	Chloroform	NI	6.3	NI	NI
54	*Syzygium jambolanum* (Myrtaceae) [Prabhakar *et al*., 2008]	Bark	Ethanol	NI	19-22	NI	NI
55	*Cassia siamea* (Fabaceae) [Prabhakar *et al*., 2008]	Bark	Ethanol	NI	19-22	NI	NI
56	*Odina wodier* (Anacardiaceae) [Prabhakar *et al*., 2008]	Bark	Ethanol	NI	11-14	NI	NI
57	*Sargassum wightii* (Sargassaceae) [Prabhakar *et al*., 2008]	Complete body	Ethanol	NI	19-22	NI	NI
58	*Caulerpa scalpelliformis* (Caulerpaceae) [Prabhakar *et al.*, 2008]	Complete body	Ethanol	NI	19-22	NI	NI
59	*Aniba rosaeodora* (Lauraceae) [Hammer *et al*., 1999]	Wood	AC	Essential Oil	NI	0.25	NI
60	*Apium Graveolens* (Apiaceae) [Hammer *et al*., 1999]	Seed	AC	Essential Oil	NI	1	NI
61	*Boswellia carterii* (Burseraceae) [Hammer *et al.*, 1999]	Resin	AC	Essential Oil	NI	1	NI
62	*Cananga odorata* (Annonaceae) [Hammer *et al.*, 1999]	Flower	AC	Essential Oil	NI	1	NI
63	*Cedrus atlantica* (Pinaceae) [Hammer *et al*., 1999]	Wood	AC	Essential Oil	NI	>2	NI
64	*Citrus aurantifolia* (Rutaceae) [Hammer *et al*., 1999]	Fruit	AC	Essential Oil	NI	2	NI
65	*Citrus aurantium* (Rutaceae) [Hammer *et al*., 1999]	Peel	AC	Essential Oil	NI	1	NI
66	*Citrus lemon* (Rutaceae) [Hammer *et al*., 1999]	Peel	AC	Essential Oil	NI	2	NI
67	*Citrus x paradise* (Rutaceae)	Peel	AC	Essential Oil	NI	1	NI

	[Hammer *et al*., 1999]						
68	*Citrus reticulate* var. *Madurensis* (Rutaceae) [Hammer *et al*., 1999]	Peel	AC	Essential Oil	NI	2	NI
69	*Commiphora myrrha* (Burseraceae) [Hammer *et al.*, 1999]	Resin	AC	Essential Oil	NI	>2	NI
70	*Coriandrum sativum* (Apiaceae) [Hammer *et al*., 1999]	Seed	AC	Essential Oil	NI	0.25	NI
71	*Cucurbita pepo* (Cucurbitaceae) [Hammer *et al.*, 1999]	Seed	AC	Essential Oil	NI	>2	NI
72	*Cupressus sempervirens* (Cupressaceae) [Hammer *et al.*, 1999]	Leaves & twigs	AC	Essential Oil	NI	>2	NI
73	*Cymbopogon citratus* (Poaceae) [Hammer *et al*., 1999]	Leaf	AC	Essential Oil	NI	0.06	NI
74	*Cymbopogon martini* (Poaceae) [Hammer *et al*., 1999]	Leaf	AC	Essential Oil	NI	0.06	NI
75	*Cymbopogon nardus* (Poaceae) [Hammer *et al*., 1999]	Leaf	AC	Essential Oil	NI	0.12	NI
76	*Daucus carota* (Apiaceae) [Hammer *et al*., 1999]	Seed	AC	Essential Oil	NI	2	NI
77	*Eucalyptus polybractea* (Myrtaceae) [Hammer *et al*., 1999]	Leaves & twigs	AC	Essential Oil	NI	1	NI
78	*Foeniculum vulgare* (Apiaceae) [Hammer *et al*., 1999]	Seed	AC	Essential Oil	NI	0.5	NI
79	*Gaultheria procumbens* (Ericaceae) [Hammer *et al*., 1999]	Herb	AC	Essential Oil	NI	0.25	NI
80	*Juniperus communis* (Cupressaceae) [Hammer *et al*., 1999]	Berry	AC	Essential Oil	NI	2	NI
81	*Lavandula angustifolia* (Lamiaceae) [Hammer *et al*., 1999]	Flower	AC	Essential Oil	NI	0.5	NI
82	*Macadamia integrifolia* (Proteaceae) [Hammer *et al*., 1999]	Nut	AC	Essential Oil	NI	>2	NI

83	*Melaleuca alternifolia* (Myrtaceae) [Hammer *et al*., 1999]	Leaves & twigs	AC	Essential Oil	NI	0.5	NI
84	*Melaleuca cajuputi* (Myrtaceae) [Hammer *et al*., 1999]	Leaves & twigs	AC	Essential Oil	NI	1	NI
85	*Melaleuca quinquenervia* (Myrtaceae) [Hammer *et al*., 1999]	Leaves & twigs	AC	Essential Oil	NI	0.25	NI
86	*Mentha spicata* (Lamiaceae) [Hammer *et al*., 1999; Sartoratto *et al*., 2004]	Herb	AC	Essential Oil: Piperitenone oxide, β-farnesene, γ-muurolene,	NI NI	0.12 >2.00	NI NI
87	*Ocimum basilicum* (Lamiaceae) [Hammer *et al*., 1999; Sartoratto *et al*., 2004]	Herb	AC	Essential Oil: 1,8-cineol, fenchone, linalool, camphor, terpin-4-ol, α-terpineol, eugenol, β-bourbonene, β-elemene, *trans*-caryophillene, β-bergamotene, α-guaiene, α-humulene, germacrene D, δ-guaiene, δ- cardiene, γ-cardiene, epi-α-muurolol, α-eudesmol, α-cadinol.	NI NI	0.5 >2.00	NI NI
88	*Ocimum gratissimum* (Lamiaceae) [Sartoratto *et al*., 2004]	Herb	AC	Essential Oil : Terpin-4-ol, *trans*-caryophillene, eugenol, germacrene D, δ- cardiene, α-cadinol.	NI	>2.0	NI
89	*Oenothera biennis* (Onagraceae) [Hammer *et al*., 1999]	Seed	AC	Essential Oil	NI	>2	NI
90	*Origanum majorana* (Lamiaceae) [Hammer *et al*., 1999]	Herb	AC	Essential Oil	NI	0.25	NI
91	*Origanum vulgare* (Lamiaceae) [Hammer *et al*., 1999; Sartoratto *et al*., 2004]	Herb	AC	Essential Oil: 1-octen-3-ol, *p*-cimene, trans-β-ocimene, γ-terpinene, α-terpinolene, *cis*-*p*-	NI NI	0.12 2.00	NI NI

				menth-2-en-1-ol, *trans*-*p*-menth-2-en-1-ol, borneol, terpin-4-ol, α-terpineol, trans-piperitol, thymol methyl ether, carvacrol methyl ether, thymol, geranyl acetate, *trans*-caryophillene, germacrene D, β-bisabolene, espatulenol, caryophillene oxide, α-eudesmol.			
92	*Origanum applii* (Lamiaceae) [Sartoratto *et al*., 2004]	Herb	AC	Essential Oil: Linalool, terpin-4-ol, cimen-8-ol, thymol methyl ether, carvacrol methyl ether,thymol, β-bourbonene, β-gurjunene, *allo*-aromadendrene, germacrene D, β-bisabolene, γ-cadinene, espatulenol, α-muurolol, α-cadinol.	NI	>2.0	NI
93	*Aloysia tryphila* (Verbenaceae) [Sartoratto *et al*., 2004]	Herb	AC	Essential Oil: 1-octen-3-ol, p-cimene, limonene, trans-β-ocimene, γ-terpinene, linalool, α-terpineol, neral, geranial, geranyl acetate, cedrene, *trans*-caryophillene, curcumene, zingiberene, δ-cadinene, espatulenol, caryophillene oxide.	NI	0.80	NI
94	*Pelargonium graveolens* (Geraniaceae) [Hammer *et al*., 1999]	Herb	AC	Essential Oil	NI	0.12	NI
95	*Pimpinella anisum* (Apiaceae)	Seed	AC	Essential Oil	NI	0.5	NI

	[Hammer *et al*., 1999]						
96	*Pimenta racemosa* (Myrtaceae) [Hammer *et al*., 1999]	Leaf	AC	Essential Oil	NI	0.12	NI
97	*Pinus sylvestris* (Pinaceae) [Hammer *et al*., 1999]	Needles	AC	Essential Oil	NI	2	NI
98	*Piper nigrum* (Piperaceae) [Hammer *et al*., 1999]	Berry	AC	Essential Oil	NI	>2	NI
99	*Pogostemon patchouli* (Lamiaceae) [Hammer *et al*., 1999]	Leaf	AC	Essential Oil	NI	0.5	NI
100	*Prunus armeniaca* (Rosaceae) [Hammer *et al*., 1999]	Seed	AC	Essential Oil	NI	>2	NI
101	*Prunus dulcis* (Rosaceae) [Hammer *et al*., 1999]	Seed	AC	Essential Oil	NI	>2	NI
102	*Thymus vulgaris* (Lamiaceae) [Hammer *et al*., 1999; Sartoratto *et al*., 2004]	Herb	AC	Essential Oil: 1-octen-3-ol, *p*-cimene, γ-terpinene, linalool, borneol, terpin-4-ol, thymol methyl ether, thymol, carvacrol, *trans*-caryophillene, γ-cadienene	NI NI	0.12 2.00	NI NI
103	*Salvia sclarea* (Lamiaceae) [Hammer *et al*., 1999]	Herb	AC	Essential Oil	NI	>2	NI
104	*Santalum album* (Santalaceae) [Hammer *et al*., 1999]	Wood	AC	Essential Oil	NI	0.06	NI
105	*Vetiveria zizanioides* (Poaceae) [Hammer *et al*., 1999]	Leaf	AC	Essential Oil	NI	0.12	NI
106	*Zingiber officinale* (Zingiberaceae) [Hammer *et al*., 1999]	Rhizome	AC	Essential Oil	NI	>2	NI
107	*Echinophora platyloba* (Umbelliferae) [Avijgan *et al*., 2006; Nourozi *et al*., 1989*]	Aerial part	Ethanol	(Flavonoid, alkaloid & saponin)*	2	NI	NI
108	*Phlomis pungens* var. *pungens* (Lamiaceae)	Dried plant	Chloroform	NI	9	NI	NI

	[Dogan *et al*., 2010]						
109	*Phlomis armeniaca* (Lamiaceae) [Dogan *et al*., 2010]	Dried plant	Chloroform	NI	15	NI	NI
110	*Tanacetum argenteum* (Asteraceae) [Dogan *et al*., 2010]	Dried plant	Chloroform	NI	12	NI	NI
111	*Pogostemon parviflorus* (Lamiaceae) [Najafi *et al*., 2011]	Leaf	Methanol Ethanol	Saponins, reducing sugars, tannins, phenols, proteins, triterpenes	10-18 8-15	2.5-10 2.5-20	NI NI
112	*Albizia lebbeck* (Fabaceae) [Maji *et al*., 2010; El-Hawary *et al*., 2011*]	Leaf	Water Acetone Benzene	(β-Carotene, linoleic acid, β-sitosterol, amino acids, tannins)*	7 13 6	0.60 0.41 0.50	0.70 0.55 0.65
113	*Cleistanthus collinus* (Phyllanthaceae) [Maji *et al*., 2010; Govindachari *et al*., 1969*]	Leaf	Water Acetone Benzene	(Ellagic acid, diphyllin, two lignin lactones, cleistanthin and collinusin)*	8 13 10	0.60 0.39 0.53	0.75 0.450.70
114	*Emblica officinalis* (Phyllanthaceae) [Maji *et al*., 2010; Bhattacharya *et al*., 1999*]	Leaf	Water Acetone Benzene	(Emblicanin A,B, punigluconin, pedunculagin)*	9 12 10	0.59 0.48 0.53	0.65 0.55 0.75
115	*Eucalyptus deglupta* (Myrtaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	4 10 9	- 0.47 0.60	- 0.55 0.85
116	*Eupatorium odoratum* (Asteraceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	8 10 13	0.60 0.50 0.45	- 0.55 0.85
117	*Oxalis corniculata* (Oxalidaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	6 4 7	- - 0.60	- - 0.65
118	*Hevea brasiliensis* (Euphorbiaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	8 12 9	0.58 0.58 0.60	0.80 0.70 0.80
119	*Lantana camara* (Verbenaceae) [Maji *et al*., 2010; Ganjewala *et al*., 2009*]	Leaf	Water Acetone Benzene	(Carbohydrates, glycolipids, phospholipids, alkaloids, phenolics, terpenoids, phycobatannins, steroid, saponin, phytosterol, tannin)*	10 13 6	0.59 0.53 0.60	0.90 0.60 0.90
120	*Adina cordifolia*	Leaf	Water	NI	5	-	-

	(Rubiaceae) [Maji *et al*., 2010]		Acetone Benzene		7 6	0.80 -	0.90 -
121	*Aegle marmelos* (Rutaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	4 4 4	- - -	- - -
122	*Asparagus racemose* (Asparagaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	4 6 5	- - -	- - -
123	*Butea frondosais* (Fabaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	4 7 4	- 0.78 -	- 1 -
124	*Curculigo orchioides* (Hypoxidaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	4 4 4	- - -	- - -
125	*Dillenia pentagyna* (Dilleniaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	5 5.5 4	- - -	- - -
126	*Lygodium pinnatifidum* (Lygodiaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	4 7 4	- 0.80 -	- 1 -
127	*Melastoma malabathricum* (Melastomataceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	4 8 7	- 0.79 -	- 0.90 -
128	*Ocimum basilicum* (Lamiaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	4 12 4	- 0.60 -	- 0.85 -
129	*Terminalia arjuna* (Combretaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	5 7 5	- 0.76 -	- 1 -
130	*Valeriana wallichii* (Valerianaceae) [Maji *et al*., 2010]	Leaf	Water Acetone Benzene	NI	4 4 4	- - -	- - -
131	*Thymus mongolicus* (Lamiaceae) [Omran *et al*., 2009]	Leaf	Hexane	NI	NI	<6.4	NI
132	*Mentha pulegium* (Lamiaceae) [Omran *et al*., 2009]	Leaf	Hexane	NI	NI	<6.4	NI
133	*Citrus lemon* (Rutaceae) [Omran *et al*., 2009]	Leaf	Hexane	NI	NI	<6.4	NI
134	*Boesenbergia pandurata* (Zingiberaceae) [Taweechaissupapong *et al*., 2010]	Yellow rhizome	Ethanol (Maceration) Hydro-distillation	NI Essential Oil: Geraniol (olefinic terpene), linalool, α-	- 15.84	- 0.5	1.25 0.5

				terpineol			
135	*Piper sarmentosum* (Piperaceae) [Taweechaissupapong *et al*., 2010; Masuda *et al*., 1991*]	Leaf	Ethanol	(1-allyl-2,6-dimethoxy-3,4-methylenedioxybenzene, 1-allyl-2,4,5-trimethoxybenzene, 1-(1-E-propenyl)-2,4,5-trimethoxybenzene and 1-allyl-2-methoxy-4,5-methylenedioxybenzene)*	10.81	-	1.25
			Hydro-Distillation	Oils	-	-	-
136	*Murraya koenigii* (Rutaceae) [Zachariah *et al*., 2009]	Stem bark	Alkaloids Coumarin Chloroform Alcohol Acetone	NI	12-19 21 11 18 20	NI NI NI NI NI	NI NI NI NI NI
137	*Embelia ribes* (Myrsinaceae) [Suthar *et al.,* 2009]	Fruits	Petroleum ether Diethyl ether Methanol Water	Benzoquinone derivative: Embelin (2,5-dihydroxy-3-undecyl-2, 5-cyclohexadiene, 4-benzoquinone) and Vilangin	NI NI NI NI	290 660 120 2140	NI NI NI NI
138	Traditional Chinese Medicine (Pseudolaric acid B, Gentiopicrin. Rhein and Alion) [Yan *et al* ., 2012]	AC	DMSO	Pseudolaric acid B, Gentiopicrin. Rhein and Alion	-	42.22	42.22
139	*Morinda citrifolia* (Rubiaceae) [Jainkittivong *et al.,* 2009; Deng *et al*., 2010*; West *et al*., 2011*]	Fruit	Aqueous	Iridoids (Deacetylasperulosidic acid and Asperulosidic acid)*	NI	40	NI

Abbreviations: Activity not found (-); Not investigated (NI); Available Commercially (AC); Zone of Inhibition in millimetre (ZOI mm); Minimum Inhibitory Concentration for 50 % inhibition (MIC_{50}); Minimum Fungicidal concentration for 50 % sensitivity (MFC_{50});. (*) in Phytoconstituent column to the respective (*) for reference in same row.

CONCLUSION

Candida albicans is the most frequent pathogenic species followed by *C. glabrata*. *Candida* species associated morbidity and mortality is reported to increase at an alarming rate in India and overseas due to its lead role in hospital acquired infections. Increasing reports on *Candida* resistance to existing antibiotics & invasive Candidosis have led the attention of many researchers to develop alternative plant based effective therapeutics.

A total of 139 plants are listed here for their properties against *Candida albicans* particularly. Appreciable anti-*Candida* properties are observed in members of the families Apiaceae, Lamiaceae, Asteraceae, Fabaceae, Bignomiaceae, Piperaceae, Zingiberaceae, Rutaceae, Poaceae, Cucurbetaceae, Meliaceae, Lauraceae, Verbenaceae, Rutaceae, Rubiaceae. Extracts from *Acacia sp.* (Fabaceae), *Aloe vera* (Xanthorrhoeaceae), *Cinnamomum zeylanicum* (Lauraceae), *Warburgia salutaris* (Canellaceae), *Syzygium aromaticum* (Myrtaceae), *Piper capense* (Piperaceae) and *Cassia tora* (Caesalpinaceae) are reported to exhibit best characteristic features of inhibiting *Candida albicans* in agar and broth media.

Studies reporting above plants (listed in the table above) as a source of effective anti Candidal drug lacks detailed experimentation that is required for thorough characterization of herbal extracts as per regulatory guidelines. Active phytoconstituents are needed to be isolated and screened for its anti-*Candida* properties like inhibition of yeast to hyphae transition, adhesion and biofilm formation mainly.

Different extracts and essential oils from the various plants are very effective to inhibit the growth of *C. albicans* in the initial experiments but they needs to be explored in adequate details in animal models along with the toxicity studies for establishing them as therapeutic modules against *Candida* species. Because of plant origin, such herbal drugs would be better choices against Candidosis for being safe, effective and inexpensive.

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