



Review Article

Medicinal Plants *Acalypha indica* and *Prosopis glandulosa* an Alternative Medication for Candidiasis

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ABSTRACT

Candidiasis is the infection caused by the species of genus *Candida*. These are thin walled, ovoid yeast cells typically 4-6 cm in size. More than one hundred fifty species are identified in that nine species are pathogenic to human beings. *Candida* and other yeast like organisms often form the normal flora of skin, mouth, vagina, intestine and known to be opportunistic pathogens in infected persons with low body defense mechanism. Patients usually with HIV infection, diabetes mellitus, drug addiction or inhaled steroids were risk cases for *Candida* infections. The development of microbial resistant to antibiotics has led the research to investigate the alternative source for the treatment of resistant strains. One possible approach is to screen local medicinal plants to get the compound, which can be directly use as antifungal agents or can serve as template for drug development. Medicinal plants have been used as an exemplary source from centuries as an alternative remedy for treating human diseases because they contain numerous active constitutes of therapeutic value. Bioactive compounds currently extracted from plants are used as medicines. Many of the plant species have traditional value and scientifically evaluated for their possible medicinal application. Here in this review we investigated the medicinal plants *Acalypha indica* and *Prosopis glandulosa* an alternative medication for candidiasis.

Keywords

Candida infections,
Medicinal plants,
Acalypha indica,
Prosopis glandulosa

Introduction

Herbal medicine is the oldest form of health care known to mankind and it will not be annex aggregation to say that use of herbal drug for human health is probably as ancient as mankind (Amita and Kalpana, 2009). India is represented by rich culture, tradition, natural biodiversity and offer unique opportunity for the drug discovery researches. Utilization of plants

for medicinal purpose in India has been documented in ancient literature (Kirtikr and Basu, 1975). The world health organization has estimated that 80% population of the developing countries is unable to afford the pharmaceutical drugs and rely on traditional herbal medicine to sustain their primary health care needs (Sankaranarayanan *et al.*, 2010). The development of microbial

resistant to antibiotics has led the research to investigate the alternative source for the treatment of resistant strains (Lata *et al.*, 2010). Various techniques have been adopted for enhancing bioactive molecules in medicinal plants. Recent advantage in the molecular biology, enzymology and fermentation technology of plant cell culture suggest that their system may become a viable source of important secondary metabolites (Mohammed Yaseen *et al.*, 2009). The valuable and in-depth knowledge about the medicinal plant in India gathered over a long period of time need to be exploited scientifically to the maximum extent.

Identification of *Candida albicans*

Candida species are thin walled; ovoid yeast cells typically 4-6 μ m in size. More than one hundred fifty species are identified in that nine are pathogenic to human beings. *Candida* and other yeast like organisms often form the normal flora of skin, mouth, vagina, intestine and known to be opportunistic pathogens infect persons with low body defense mechanism (Yung- Liang, 2003). *Candida albicans* grow at 37°C and produce germ tubes and chlamydospores on corn meal agar and blood plasma. Negative results are shown for pellicle growth and gas on Sabouraud's broth and for ascospores formation, nitrate production and growth on seed agar tests, but growth occurs on Eosin methylene blue agar with tetracycline (Gow, 1997). *Candida* is also able to assimilate sucrose, dextrose, galactose, maltose, trehalose and xylose but not lactose, raffinose and cellobiose. These characters are the typical one used for *Candida albicans* confirmation. When the suspected strains of *Candida albicans* is inoculated with human serum the formation of germ tube was seen as long tube like projection extending from the yeast cells. The germ

tube forms within two hours of incubation in *Candida albicans*. The carbohydrate assimilation test for *Candida albicans* is positive for dextrose, maltose, sucrose, galactose, xylose and trehalose. At the same time, the tests are negative for lactose, melibiose, cellobiose, inositol, raffinose and ducitol. Similarly, the carbohydrate fermentation tests for *Candida albicans* are dextrose, maltose, galactose and trehalose were positive but negative for fermentation of sucrose and lactose.

Vulvovaginalitis candidiasis

Thrush is caused by *Candida albicans*, which may be present in the vagina of up to 20% of sexually active women initially but may become pathogenic when conditions of vagina changes, particularly when there is a rise in vaginal pH or an excess of glycogen that has not been converted to lactic acid by *Lactobacilli* (Alison, 2000). Symptoms of vaginitis involve itching, burning, cheesy white scant discharge is uncommon (Sobel, 1997). It has been reported that in *Candida albicans* the cytosolic enzyme and enolase act as an immuno-dominant antigen (Mitsuake *et al.*, 1994). Vaginal thrush is characterized by typical white lesion developed on the epithelial surface of vagina, vulva and cervix (Saravana Bhavan *et al.*, 2010). Water change is the most common cause of vaginitis. Physical examination finding include a vagina and labia that are usually erythematous, a thick curd like discharge and a norma cervix upon speculum examination (Sobel *et al.*, 2003). Candidiasis infection caused by *Candida albicans* can be acute or chronic, superficial or deep, and its clinical symptoms are so wide that a more specific definition cannot be made (Changdeo, 2014; Francois *et al.*, 2013). Various identification tests like growth pattern, sugar fermentation, urease production and development of germ tube in

human serum confirms the presence of *Candida albicans* (Al-Fattani and Douglas, 2006). *Candida* is harmless initially, but may become pathogenic when the conditions in the vagina change, particularly when there is a rise in vaginal pH or an excess of glycogen that has not been converted to lactic acid by *Lactobacilli* (Calderone and Fonzi, 2001).

Risk factors

Patients with diabetes are at increased risk of developing vulvovaginal candidiasis (VVC). Unlike non-diabetic women these patients have a higher proportional of colonization (Wu et al., 1996). Patients usually with a history of HIV infection, diabetes mellitus, drug addiction or inhaled steroids, and with low body defense mechanisms are risk cases for *Candida* infections (Mavor et al., 2005). Candidiasis is caused by infection with species of the genus *Candida* is a ubiquitous fungus that represent the most common fungal pathogens that affect human and there is a positive correlation between smoking and candidiasis (Bader et al., 2003). *Candida* species produce a wide spectrum of diseases, ranging from superficial mucocutaneous to invasive illness (Deshpande et al., 2010). *Candida albicans* enolase with the plasmid system may contribute to invasive of the tissue barrier (Jong, 2008). Antifungal susceptibility of Vaginal yeast isolates in a rural community of India, since majority of *Candida albicans* isolates were susceptible to Fluconazole, its use is continued for empirical therapy of uncomplicated *Candidal vulvovaginitis* in the community (Masia Canuto et al., 2000).

Drug resistant

The antibiotics used for the treatment are azoles such as Amphotericin, Fluconazole, Itraconazole, Caspofungin, Vericonazole,

Ketaconazole and 5-Fluorocytosine (Wayne, 2004). One of the major increases in the *Candida* is the development of its resistant strains to azoles drugs used in the prophylaxis and treatment of candidiasis. The nature of the resistant to a few drugs has been identified as related to altered related transport, modification of an enzyme and change in the membrane composition (Segal and Elad, 1998). However a broad spectrum identified initially as combined resistance to benomyl and Methotixate and later as resistance to four additional antigens, appeared to be an inherent characteristic of the species so therefore there is a real need for next generation safer and more potent antifungal agents. An antibiogram test is reported that the antibiotics used against *Candida* spp Amphotericin B, Fluconazole, Caspofungin, Itraconazole, 5-Fluorocytosine and Voriconazole are used as drug of choice for treatment (CLSI, 2004). *Candida albicans* shows susceptibility pattern of about 99% to Amphotericin B, 97% to Fluconazole, 99% to 5-Fluorocytosine and 94% to Voriconazole (Kothavade et al., 2010; Angiolella et al., 1996). However a broad spectrum resistance initially as combined resistance to benomyl and methotrixate, then later on resistant to four additional agents appeared to be an inherent characteristic of the species and are shown to be determined by a single gene encoding a polypeptide of 564 aminoacid with a series of features typical of prokaryotic and eukaryotic transporter protein and multidrug resistant efflux pumps (Shahid et al., 2006). Antifungal susceptibility of vaginal yeast isolates in a rural community of India, since majority of *Candida albicans* isolates were susceptible to Fluconazole, its use may be continued for empirical therapy of uncomplicated candidal vulvovaginitis in the community. Use of alternative agents like Boric acid and Flucytosine may be considered when treating vulvovaginitis

caused by non-albicans (Srujana et al., 2007). The over expression of the multidrug transporter Cdr1p (*Candida* drug resistance protein 1), a member of the ABCI (ATP Binding Cassette) transporter super family (1-3), is an account for a clinically significant mechanisms of azoles resistance in the pathogenic yeast *Candida albicans* (Willis et al., 2001). This is especially clear in Fluconazole resistant clinical isolates of *Candida albicans*, where enhanced expression of Cdr1p promoter efflux of therapeutic azoles, thus facilitating cell survival. Cdr1p, like other ABC transporters, uses ATP hydrolysis to power the transport of substrates across the membrane (Sudhanshu et al., 2007).

Prevalence

Approximately three-quarters of all women experience at least one episode of vulvovaginal candidiasis during their lifetime nearly half of them suffer from multiple episode. The majority of cases of vulvovaginal candidiasis are caused by *Candida albicans*. *Candida* species are currently the fourth leading cause of hospital acquired blood stream infections, reaching a mortality rate of up to 35-40% for systemic or disseminated infections. Among all *Candida* species *Candida albicans* is still the most frequently isolated species, about 15–20% in Europe (Mendes et al., 2007). Vaginal candidiasis is the second most common cause of vaginitis after anaerobic bacterial vaginitis. Among various groups vaginal candidiasis is most common in pregnant women having incidence of 66.1% followed by *Candida glabratai* 44.1% (Crowe et al., 2003). It is estimated that out of 1050 women Aligarh, India, 20.47% were positive for *Candida* spp. In that *Candida albicans* accounted for 46.9%. The most common signs and symptoms in 215 women with positive were pruritus with or without vaginal discharge and vaginal erythema

(Sardi et al., 2011).

Medicinal plants

One possible approach is to screen local medicinal plants to get the compound, which can directly use as antifungal agents or can serve as template for drug development (Vaghasiya and Chanda, 2009). The plant is selected according to its availability and ethanobotanical significance in the treatment of opportunistic mycosis. The use of medicinal plants as a source for relief from illness can be treated back over five millennia to written documents of the early civilization in china, India and the Near East but it is doubtless an art as old as mankind. The potential for higher studies as source for new drugs is still largely unexplored. Among the estimated 250,00-500,00 plant species, only a small percentage has been investigated phytochemically and fraction submitted to biological or pharmacological screen is even small (Mahesh and Sathish, 2008). Established and tested drugs from medicinal plant heal various diseases and disorder to which there are no solutions from modern medicine even today and hence ethanotherapeutics has been reported. Since time commercial Ayurvedha and Siddha systems of medicine are the traditional heritage of India wherein diverse plant has been used (Rahmatullah et al., 2009). India is blessed with two (Eastern Himalayas and Western Ghats) of the eighteen world's hotspots of plant diversity and is seventh among the sixteen-mega diverse countries, where 70% of the world's plant species occurred collectively. Medicinal plants have been used as an exemplary source of centuries as an alternative remedy for treating human diseases because they contain numerous active constitutes of therapeutic value (Ezzat, 2001). There is an urgent need to search for alternative to synthetic antibiotics.

The revolution of the discovery of new groups of antimicrobial peptides makes natural antibiotics, the basic element of a novel generation of drug for the treatment of bacterial and fungal infections (Tariq and Reyaz, 2012). The global demand for herbal medicine is large, growing rapidly and is the most exclusive source saving drugs for majority of the world's population. Bioactive compounds currently extracted from plants are used as medicines have traditional value and scientifically evaluated for their possible medicinal application (Sangeetha *et al.*, 2010). An increasing prevalence infections caused by newer emerging fungal pathogens have been detected in humans, although it appeared that many drugs are available for the treatment of systemic and superficial mycosis clinical usefulness is hampered by drawbacks associated with safely or efficiently (Karkowska-Kuleta *et al.*, 2009). Plants have been used as source of medicine since the dawn of civilization established tested drugs from medicinal plants heals various diseases and disorders to which there is no solution from medicine even today and hence ethanotherapeutics has been reported (Ahmad *et al.*, 1989).

Medicinal plants used against candidiasis

Medicinal plants have been used as an exemplary source for centuries as an alternative remedy for treating human diseases because they contain numerous active constituents of therapeutic value (Gayathri and Kannabiran, 2009). The development of microbial resistant to antibiotics has led the research to investigate the alternative source for the treatment of resistant strains. Presently 80% of the world population relies on plant derived medicines, serve as first line of defense in maintaining health and computing many diseases.

Role of *Acalypha indica* as medicinal plant

The *Acalypha indica* belongs to the following taxonomic classification

Kingdom : Plantae
Class : Magnoliopsida
Order : Euphorbiales
Family : Euphorbiaceae
Sub family : Acalyphoideae
Genus : *Acalypha*
Species : *Acalypha indica* linn

It is commonly known as kucinggalak or Rumputlilis. Kuppaimeni in Tamil and Kuppaikunjan in Malayalam. It is a main weed in many part of Asia including India, Pakistan, Yemen, Srilanka throughout tropical Africa and South America (Ramachandran, 2008). It is an annual herb, about 80cm height (Buskill, 1985). This plant is used as diuretic, antihelminthic and for respiratory tract problem such as bronchitis, asthma and pneumonia (Varier, 1996). The root of *Acalypha indica* is used as laxative and leaves for scabies and other cutaneous disease, this plant has antimicrobial activity against several Gram positive bacteria (Govindarajan *et al.*, 2008). This plant has been extensively in herbal medicine in many tropical and subtropical countries reported that the antimicrobial activity of water, ethanol and chloroform extracts of *Acalypha indica* was tested against four bacterial and fungal strains using the disc diffusion method (Krishnaraj *et al.*, 2010). The antifungal activity is more pronounced only in chloroform extracts when compared to standard antibiotics such as Ketoconazole, Itraconazole and Fluconazole. Findings from the current study support the use of *Acalypha indica* in traditional medicine for the treatment of various bacterial and fungal infections (Somchit *et al.*, 2010). Major phytochemical identified from *Acalypha indica* are

aciphine, cyanogenic glycosides, inositol, resin, triacetamin and volatile oils (Winter and Griffith, 1998). *Acalypha indica* has antibacterial activity against several gram positive bacteria, analgesic, anti-inflammatory effects and antifungal activity (Johnson *et al.*, 1995). The maximum antifungal activity of *Acalypha indica* plant salt was shown against *Candida albicans* and *Cryptococcus neoformans*, followed by *Aspergillus flavus* in higher concentrations (Suresh *et al.*, 2009).

Role of *Prosopis glandulosa* as medicinal plant

The *Prosopis glandulosa* belongs to the following taxonomic classification

Kingdom : Plantae
SubKingdom: Tracheobionta
Division : Magnoliophyta
Class : Magnoliopsida
Subclass : Rosidae
Order : Fabales
Family : Fabaceae
Genus : *Prosopis*
Species : *Prosopis glandulosa*

Prosopis glandulosa is commonly used to treat infections, open wounds, dermatological ailments, anti-acid can treat digestive problems and its aqueous extract has antibacterial as well as antiseptic properties (Uniyal *et al.*, 2006). The phytochemicals of *Prosopis glandulosa* such as S-hydroxytryptamine have anti-depressant activity, apigenin have anti-allergic, anti-bacterial, anti-dermatic, anti-inflammatory and anti-viral activity, isorhamnetin-3-diglucoside has hepatoprotective activity, L-arabinose and quercetin have analgesic, anti-allergic, anti-bacterial, anti-diabetic, anti-inflammatory and anti-viral activity (Abdur Rahman *et al.*, 2011). The plant *Prosopis glandulosa* is

selected according to its availability and ethnobotanical significance in the treatment of opportunistic mycosis a choice of treatment (Burkhart, 1976; Kanthasamy *et al.*, 1989). *Prosopis glandulosa* is commonly used to treat infections, open wounds, dermatological ailments, acting much as an anti-acid, it can also treat digestive problems and antiseptic properties (Uddin *et al.*, 2006). The bark and roots of *Prosopis glandulosa* also contain alkaloids. The plant contain 80% carbohydrates, 13% protein 25% fiber and 3% fat (Samoylenko *et al.*, 2009).

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