Antifungal Activity of Brazilian Medicinal Plants against Candida Species

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http://dx.doi.org/10.5772/intechopen.80076

Abstract
Due to the resistance of Candida sp. to the usual antifungal, the demand for active principles found in the plants has been the target of diverse studies around the world. There are few in vivo and human studies on the antifungal activity of medicinal plants in the mouth. Native and imported medicinal plants, used by the Brazilian population for traditional medicine use, are the subject of study in this chapter. Thirty-eight Brazilian plants were related to information on species, family, name, used part, and medical indication of popular use. All the species mentioned had their extracts tested in vitro against C. albicans, C. tropicalis, C. krusei, C. parapsilosis, among other species that occur more frequently in the mouth. In the articles consulted, there is a great variation in Candida species tested and in minimum inhibitory concentration. The in vitro studies serve as information for the continuity of studies on the best performing plants, validate the popular belief about the use, and provide subsidies for the development of new products that are effective in the control of oral and systemic candidiasis and that are cheap and accessible for the population.

Keywords: Brazilian medicinal plants, Candida sp., oral candidiasis, minimum inhibitory concentration

1. Oral candidiasis—by Elizete Maria Rita Pereira/Vagner Rodrigues Santos

The most common fungal pathogens detected from the oral cavity are Candida sp. and their transition of harmless commensals to pathogenic microorganisms is often related to decrease immunity. Often, candidiasis occurs in a localized and superficial manner in the oral cavity,
but it can be systemic or invasive and even lead to death in immunocompromised individuals [1, 2]. Like other pathogenic fungi, *Candida* spp. present dimorphism in the yeast and pseudohyphatic forms. The hyphal form is associated with epithelial cell invasion and thus causing tissue damage [3]. *Candida* spp. has other virulence factors such as adherence, production of tissue-damaging hydrolytic enzymes such as proteases, and the biofilm formation in host tissue and in medical devices [4]. Several predisposing factors, local and systemic, may result in the transition from yeast Candida to the hyphal form (pathogenic). Local factors include the use of prostheses, corticosteroid inhalers, and xerostomia, while systemic factors include immunosuppressed states as human immunodeficiency virus—HIV for example. Psoriasis, recently, was described as a predisposing factor for oral candidiasis [5].

The type of *Candida* spp. most commonly isolated from the oral cavity is *C. albicans*, which occurs in both healthy and diseased individuals [1, 6, 7]. Nonalbicans species were also isolated from the oral cavity of immunocompromised patients, such as *C. glabrata*, *C. krusei*, *C. parapsilosis*, *C. tropicalis*, *C. guilliermondii*, and *C. dubliniensis* [8]. Protective immune response can be induced by Candida in the host that allows its own survival. Immunocompetent adults, usually, present acquired immunity underlying the fungus that prevents the progression of oral colonization to symptomatic infection. Integrity of the mucosa is important for oral health because normally it prevents the invasion of microorganisms, as well as macromolecules, which may be antigenic [9].

1.1. Main types, diagnosis, and treatment of oral candidiasis

Candidiasis is an acute or chronic infection produced by *Candida* sp., often, limited to the skin and mucous membranes, but can produce a severe systemic disease in immunocompromised patients [3]. It may exhibit various clinical patterns such as the four primary oral forms: pseudo-membranous candidiasis (thrush), acute erythematous oral candidiasis, chronic erythematous oral candidiasis, and chronic hyperplastic candidiasis (Table 1). These primary forms of candidiasis are also associated with lesions called secondary forms of candidiasis, such as angular cheilitis, median rhomboid glossitis, and *Candida* sp.-associated prosthesis stomatitis [10].

Diagnosis of oral candidiasis is established by identification of clinical signs and symptoms in conjunction with the presence of Candida organisms in the examination of an injury smear, biopsy examination containing hyphal form in the epithelium (Schiff’s Periodic Acid), or positive culture and serological tests [11–13].

Generally, the drugs of choice for localized, uncomplicated candidiasis in patients with normal immune function are topical antifungal agents (Figure 1). These agents can achieve elevated levels of concentration in the oral epithelium [14]. Azoles act inhibiting the lanosterol 14-α-demethylase (enzyme involved in ergosterol biosynthesis) activity 14-α-demethylase (enzyme involved in ergosterol biosynthesis) and disrupt the cell membrane. The resistance to azole, generally, can be observed in HIV/AIDS patients receiving treatment for pre-HAART oral or esophageal candidiasis, for example. The resistance mechanisms of *C. albicans* include mutations that result in increased expression of efflux pumps (CDR1P, CDR2P, and MDR1P) and mutations in the target ERG11 drug [15].

Polyenes act by direct binding to ergosterol within the membranes of fungal cells, therefore, inducing the leakage of cytoplasmic content and leading to the death of microorganism.
Formulations of nystatin or amphotericin B are used for 4 weeks [11, 14]. Resistance was observed in case reports of cancer patients on chemotherapy and those who have received long-term prophylactic therapy. The mechanism of Candida resistance to the polyenes are not yet known, but seem to involve changes in the cell membrane composition [15].

Echinocandins are noncompetitive inhibitors of the β-1,3 glucan synthase encoded by the FKS1 gene of C. albicans, which leads to the formation of fungal cell walls with impaired structural integrity, leading to osmotic lysis. Resistance is associated with acquired or intrinsic
FKS1 point mutations [15]. Flucidosycin is a pyrimidine analogue, which is transported to fungal cells by cytosine permeases. After this, 5-fluorouracil and phosphorylation of 5-fluorodeoxyuridine monophosphate are deaminated. This nucleotide acts by inhibiting thymidylate synthase and interferes with DNA synthesis [14]. Mutations in the cytosine-permease FCY2 gene or the cytosine-deaminase gene FCY1 are the most common causes of drug resistance. To avoid this increased resistance, flucytosine is almost always administered to patients in conjunction with amphotericin B [15]. Griseofulvin, first isolated from griseofulvin, first isolated from *Penicillium griseofulvum*, inhibits the fungal mitosis to act by disrupting the production of microtubules in the spindle and cytoplasm [14].

Antifungal systemic agents are indicated in fungemia when found in low immunity or immunodeficiency, high agranulocytosis, cancer patients or patients with intravenous catheters [11]. Worldwide, an increase in the number of antifungal resistant yeasts is recognized. An important factor in contribution to human candidiasis is the ability of *Candida* species to form drug-resistant biofilms [4]. The antifungal resistance can occur by different mechanisms, such as the reduction of the intracellular accumulation of the drug, decreased affinity of the target by the drug, and neutralizing the effect of the drug. Depending on the mode of action of the antifungal compounds, the mechanism of resistance will be different [14].

The search for new antifungal agents and the characterization of new targets that are more appropriate and efficient have been proposed [4]. Potential alternative therapies include the use of new active principles obtained from different general sources, such as natural products, in particular, the plants that contain several components that are important sources of biologically active molecules [14].

**2. Brazilian medicinal plants tested against *Candida* spp.—by Vagner Rodrigues Santos**

**2.1. Introduction**

The search for therapeutic applications of medicinal plants and their derivatives has grown in the past years throughout the world. Several studies have been carried out in order to evaluate new biological properties from the biodiversity. The discovery of new antimicrobial components is of great relevance, particularly for dentistry, since bacterial and fungal infections of the oral cavity are a relatively common problem: *Candida albicans* is an opportunistic yeast commonly identified in denture stomatitis and other oral candidosis clinical forms [12].

These are examples of infectious conditions of the mouth, and the resistance to antimicrobials in clinical cases has stimulated the search for natural agents as alternative treatments for the mouth infectious conditions. In Brazil, local communities use plants and their extracts for different medicinal purposes and take advantage of the availability of these plants and the low cost for product preparation. Plants have been used as antimicrobial, anti-inflammatory, wounds scarring, and antihemorrhagic agents, just to mention a few [16].

Medicinal plants continue to be widely used in rural and urban areas of Brazil. However, the intense miscegenation of crops over the last few centuries has more popularized the use of
exotic native Brazilian plants and plants imported from other countries in popular medicine, especially in the southcentral part of the country. Most of these species were introduced by the Europeans and Africans, and are usually used according to the traditions of their places of origin [15, 16]. The growth of the pharmaceutical industry during the second half of the last century also distanced the Brazilian population from traditional medicine based on native plants. In the mid-1970s, for example, commercial pharmacies had lost their importance as the pharmaceutical industry completely dominated the drug market. This period was also marked by intense repression of mysticism, including the traditional use of medicinal plants. These facts are aggravated also by the continuous destruction of the rich Brazilian ecosystems, a process initiated with the exploration of Brazilwood by the Portuguese. As a consequence, remedies prepared with native plants, especially those of Amerindian origin, are now little known or used [16].

The Brazilian territory has about 20% of the world’s biodiversity, including plants, which serve as raw materials for the production of herbal medicines and other products. The great cultural and ethnic diversity of Brazil is responsible for the knowledge transmitted over generations on the management and use of medicinal plants [17]. The high frequency of infections by the *Candida* species, as well as the occurrence of resistance to the usual antifungal, either in the hospital environment or in domestic use, as well as the increasing number of immunocompromised patients puts us in check and leads us to search for new active principles originated from medicinal plants that are effective in the control of microorganisms [18].

Several plants have been studied in Brazil based on popular use, mainly by rural communities [16].

The antifungal activity observed in some plants may be related to the presence of flavonoid glycosides and tannins, components that have antimicrobial and anti-inflammatory properties [19]. There is a growing interest in the use of tannins as antimicrobial agents. The activity of tannins against bacteria and yeasts can be measured by their action on the membranes, since they can cross the cell wall, composed of polysaccharides and proteins, and bind to its surface [20].

Studies with natural products generate difficulties regarding the comparison of results. This situation is due to the different presentations of the products used as tincture, ethanolic extract, aqueous extract, essential oil, among others, as well as the various methodological criteria employed [21] and also the different forms of phytotherapeutic presentation, among them, oral solutions, gel, and tea by decoction. The greater or lesser biological activity of the essential oils has been shown to be dependent on the composition of their chemical constituents, such as citral, pinene, cineole, carvophyllene, elemeno, furanodiene, limonene, eugenol, eucalyptol, and carvacrol. These constituents are responsible for the antiseptic, antibacterial, antifungal, and antiparasitic properties [22].

The mode of extraction of the active principles can influence significantly the antimicrobial activity. Biosynthesis of the constituents of a plant is strongly affected by the environment, harvest and postharvest, rainfall, temperature, luminosity, and humidity [23].

The mechanisms of action of medical plant extents on *Candida* spp. are still poorly studied. Several mechanisms of action have been proposed from the rupture of the cellular membranes, which several mechanisms of action have been proposed from the rupture of the cellular membranes, which seems to interrupt the cell cycle through the synthesis of proteins and alteration of the yeast DNA [24].
The most common microbiological methods for testing plant-derived products such as extracts, resins, and essential oils are agar diffusion tests and liquid-liquid tests such as macrodilution and microdilution [25]. The techniques of application of the plant antimicrobial substance in the diffusion method are by means of disc, stainless steel, or glass cylinders and agar perforation. The agar diffusion test, also called plaque diffusion, is a physical method in which a microorganism is challenged against a biologically active substance in solid culture medium and relates the size of the growth inhibition zone of the challenged microorganism [25, 26]. The application of the diffusion method is limited to fast-growing microorganisms, which are aerobic or anaerobic. The evaluation is comparative against a reference biological standard (positive control), and the zone or halo of inhibition of growth is measured starting from the circumference of the disc or well, to the margin where there is growth of microorganisms [27]. According to the size of the halo, the microorganisms can be classified as: sensitive, when the diameter of the zone of inhibition is greater or no more than 3 mm less than the positive control; moderately sensitive, halo greater than 2 mm, but smaller than the positive control of more than 3 mm; and resistant, diameter equal to or less than 2 mm. As a positive control, a standard antimicrobial is used, and as a negative control, the solvent is used for the dissolution of the extracts [28–32]. The recommended incubation conditions are 35–37°C for bacteria for 24 to 48 hours and for fungi from 25 to 27°C for 48 to 72 hours [33–39]. These tests serve to define the minimum inhibitory concentration that quantifies the lowest concentration of the product capable of inhibiting the growth of microorganisms [40–46] (Table 3).

Table 2 shows the species, families, popular names, and used parts of plants for the various applications in traditional medicine.

| Herbs                                      | Family          | Local popular name                             | Used source       | Medical use                  | Ref.  |
|--------------------------------------------|-----------------|------------------------------------------------|-------------------|------------------------------|-------|
| *Allium sativum* L.                        | Liliaceae       | Garlic                                         | Bulb              | Antimicrobial, healing, antioxidant, antitumor | [47, 48] |
| *Anacardium humile* L.                     | Anacardiaceae   | Cajuzinho-do-cerrado, little cuckoo           | Shells, sheets, pulp | Antifungal, anti-inflammatory, hypoglycemic antioxidant, antimicrobial antiparasitic | [49, 50] |
| *Anadenanthera colubrina* (Vell) Brenan    | Fabaceae        | Angico branco, white Angico                   | Shells, resin     | Healing, anti-inflammatory, antimicrobial | [51, 52] |
| *Annona crassiflora* Mart.                 | Annonaceae      | Araticum                                       | Shells, sheets, fruits | Antimicrobial cytotoxicity   | [53, 54] |

Table 2
| Herbs                          | Family        | Local popular name | Used source | Medical use                                | Ref.          |
|-------------------------------|---------------|--------------------|-------------|--------------------------------------------|---------------|
| *Arrabidaea chica* (Hum. & Bonpl.) B. Verlot | Bignoniaceae  | Crajiru            | Sheets, shells | Anti-inflammatory, Antimicrobial, Antihypertensive, antitumoral | [55, 56]      |
| *Azadirachta indica* A. Juss  | Meliaceae     | Neem, nim          | Oil, flowers, leaves, seeds, bark | Antimicrobial, insecticide, antimalarial | [57, 59]      |
| *Baccharis dracunculifolia* DC | Asteraceae    | Rosemary, broom    | Sheets, flowers, stalk | Antimicrobial, antioxidant, antitumoral, healing | [38, 60, 61] |
| *Baccharis trimera* (Less.) DC | Asteraceae    | Carqueja           | Flowers sheets, oil | Antioxidant, antihepatotoxic, anti-inflammatory | [62, 63]      |
| *Calendula officinalis* L.    | Asteraceae    | Calendula          | Flowers      | Anti-inflammatory, healing, antimicrobial   | [64, 65]      |
| *Ceiba speciosa* (A.St-Hil) Ravena | Malvaceae    | Paineira           | Shells, sheets | Antiematism, antihypertensive, antimicrobial | [66, 67]      |
| *Centaurium erythraea* Rafn    | Gentianaceae  | Centaurea          | Shells, sheets | Digestive, emetic, febrifuge, hepatic, antioxidant, anti-inflammatory | [49, 68]      |
| *Chrysobalanus icaco* L.      | Chrysobalanus | Ajiru              | Sheets       | Antimicrobial, anti-inflammatory, antitumoral | [71]          |
| *Coriandrum sativum* L.       | Apiaceae      | Coriander, coentro | Sheets, seeds | Antibacterial, antioxidant, hepatoprotective, anticonvulsivant | [69, 70]      |
| *Croton campestris* (A. St-Hill.) | Euphorbiaceae | Canopy, velame     | Oil, barks, root | Anti-inflammatory, antimicrobial, antioxidant | [49, 72]      |
| *Curatella americana* L.      | Dilleniaceae  | Sambaiba           | Sheets       | Antimicrobial, anti-inflammatory, antiulcerogenic, antihypertensive | [73, 74]      |
| Herbs                        | Family          | Local popular name | Used source | Medical use                                      | Ref.                   |
|------------------------------|-----------------|--------------------|-------------|-------------------------------------------------|------------------------|
| *Dalbergia ecastophyllum* (Linn.) Taub. | Leguminosae     | Rabo-de-bugio      | Resin, sheets | Antitumoral, antimicrobial, antioxidant, anti-inflammatory | [75, 76] |
| *Drimys winteri* (J.R.Forst & G. Forst) | Winteraceae     | Casca d’anta       | Bark        | Antifungal, antibacterial, antioxidant          | [77, 78] |
| *Eugenia dysenterica* ex DC Mart. | Myrtaceae       | Cagaita            | Leaves, barks | Antidiarrhoeic, antileukemic                  | [79, 80] |
| *Eugenia uniflora* L.       | Myrtaceae       | Pitanga            | Leaves      | Diarrhea, fever, diabetes, inflammation, headache | [81, 82] |
| *Equisetum arvense* L.      | Equisetaceae    | horsetail          | Sheets, bark | Antioxidant, anti-inflammatory, antimicrobial, antitumoral | [83, 84] |
| *Glycyrrhiza glabra* L.     | Fabaceae        | Licorice Alcacuz   | Root, rhizome | Antioxidant, anti-inflammatory, antistoeoporotic | [85, 86] |
| *Hymenaea courbaril* L.     | Leguminosae     | Jatobá             | Sap, peel   | Antimicrobial, anti-inflammatory, antitumor bronchitis, antidiarrheal | [87, 88] |
| *Jacaranda cuspidifolia* Mart. | Bignoniaceae    | Rosewood, Jacarandá | Barks, leaves, resin | Antimicrobial, anti-inflammatory, antitumor | [89, 90] |
| *Lafoensia pacari* (A.St-Hill). | Lythraceae      | Mangava brava      | Stem bark   | Anti-inflammatory analgesic                   | [91, 49] |
| *Lippia sidoides* Cham.     | Verbenaceae     | Rosemary-pepper, Alercrim-pimenta | Leaves, barks | Antinociceptive, anti-inflammatory antimicrobial | [60, 92] |
| *Malva sylvestris* L.       | Malvaceae       | Mauve, malva       | Sheets, flowers | Cough, anti-inflammatory healing           | [93, 94] |
| *Maytenus salicifolia* Mart Ex Reissek | Celastraceae    | Holy Thorn, Espinheira santa | Sheets | Antiseptic, dyspepsia, antiulcer       | [95, 96] |
| *Melaleuca alternifolia* Cheel | Myrtaceae       | Melaleuca           | Essential oil | Antiseptic, anti-inflammatory, antifungal | [87, 97, 98] |
Table 2. Relation of Brazilian medicinal plants tested in vitro against Candida species.

| Herbs                                      | Family          | Local popular name | Used source | Medical use                                      | Ref.       |
|--------------------------------------------|-----------------|--------------------|-------------|-------------------------------------------------|------------|
| Mentha piperita L.                         | Lamiaceae       | Peppermint, H ortelâ–pimenta | Sheets      | Expectorant, carminative, anti-inflammatory antimicrobial | [55, 92]   |
| Myroxylon peruiferum L.f.                  | Fabaceae        | Cabreúva           | Bark, fruits| Anti-inflammatory, anti-headache, antifungal     | [87, 99]   |
| Psidium guajava L.                         | Myrtaceae       | Guava tree goiabeira | Leaves, fruits | Antioxidant, antimicrobial, anti-inflammatory | [81, 100] |
| Punica granatum L.                         | Punicaceae      | Pomegranate Româ    | Bark, peel, pericarp, leaves, juice | Antioxidant, anti-inflammatory, antimicrobial, anticarcinogenic | [20, 101, 102] |
| Ricinus communis L.                        | Euphorbiaceae   | Castor mamona      | Aerial parts | Antidiabetic, antifertility, anti-inflammatory antimicrobial, antioxidant | [103, 104] |
| Sapindus saponaria var. drummondii (Hook. & Arn.) L. Benson | Sapindaceae | Soapberry          | Leaves, fruits, barks | Diuretics, expectorants antifungal, antioxidant | [105, 106] |
| Schinus terebinthifolius Raddi             | Anacardiaceae   | Aroeira            | Fruits, leaves, stem bark, essential oil | Antioxidant, anti-inflammation antimicrobial, antifungal, antiulcer | [69, 107] |
| Stryphnodendron adstringens (Mart) Coville, 1910 | Fabaceae       | Barbatimão         | Bark leaves | Anti-inflammatory, cicatrizant, antimicrobial | [108–110] |
| Visonia guianensis (Aubl.) Pers.           | Clusiaceae      | Sealing wax Pau-de-lacre, Resin, sheets, stalk | Anti-inflammatory, antifungal | [87, 111, 112] |
| Ziziphus joazeiro Mart.                    | Rhamnaceae      | Juazeiro           | Leaves, fruits, bark, root. | Anti-inflammation, antimicrobial, healing | [87, 113] |

The table lists the native species and those imported or brought to Brazil.

*Ref.—References.
| Herbs                                      | Active compounds                                                                 | Microorganism | MIC: μg/mL | Ref.   |
|-------------------------------------------|----------------------------------------------------------------------------------|---------------|------------|--------|
| *Allium sativum* L.                       | Quercetin, cyanidin, allistatin, allicin, ajoene                                 | *C. albicans* | 0.125      | [47, 48]|
|                                           |                                                                                  | *C. glabrata* | 0.312      |        |
|                                           |                                                                                  | *C. tropicalis* | 1.56      |        |
|                                           |                                                                                  | *C. parapsilosis* | 12.5    |        |
| *Anacardium humile*                       | Tannins, saponins, flavonoids amentoflavone                                      | *C. albicans* | 1.50       | [114, 49, 50]|
| *Anadenanthera colubrina* (Vell)          | Tannins, flavonoids                                                             | *C. albicans* | 0.031      | [115, 51, 52]|
| *Annona crassiflora* (Mart.)              | Antioxidant, tannins                                                            | *C. albicans* | 2.0        | [54, 116]|
|                                           |                                                                                  | *C. tropicalis* | 0.25      |        |
|                                           |                                                                                  | *C. krusei*   | 0.5        |        |
| *Arrabidaea chica*                        | Isosculetellaein, 6-hydroxyxuteolin, hispidulin, scutellarein, luteolin, apigenin, anthocyanins, coumarins, flavonoids, saponins, tannins, triterpenes | *C. albicans*, *C. dubliniensis*, *C. parapsilosis*, *C. tropicalis*, *C. krusei*, *C. guilliermondii*, *C. utilis*, *C. lusitaniae*, *C. glabrata*, *C. rugosa* | 0.007/0.015 | [55, 56, 102]|
| *Azadirachta indica*                      | Nimonol, mahmoodin, naheedin                                                    | *C. albicans* | 1000/500   | [58, 117, 118]|
| *Baccharis dracunculifolia*               | Artepillin C, baccharin, kaempferide, drupanin, p-coumaric acid, culifolin, caffeic acid phenethyl ester, chlorogenic acid, kaempferol, pinocembrin, naringenin, chrysin | *C. albicans*, *C. glabrata*, *C. albicans*, *C. tropicalis*, *C. stellatoidea*, *C. krusei*, *C. lusitaniae* | 0.350, 0.43, 20–320 | [24, 38, 92, 119]|
|                                           |                                                                                  | *C. glabrata* | 0.43       |        |
|                                           |                                                                                  | *C. albicans* | 2.0        | [120, 121]|
| *Baccharis trimera*                       | Flavonoids, phenolic acids, quercetin, luteolin, nepetin or eupafolin, apigenin, hispidulin, phytoalexin | *C. albicans* | 0.2        | [66, 67]|
| *Calendula officinalis* L.                | Quercetin, hyperosides, α-cadinol, gamma-cadinene, 1,2,3-cadinatriene, α-muurolol | *C. albicans* | 11.0 a 30 | [64, 65]|
|                                           |                                                                                  | *C. parapsilosis* |        |        |
|                                           |                                                                                  | *C. dubliniensis* |        |        |
|                                           |                                                                                  | *C. glabrata* |            |        |
| *Ceiba speciosa* (A.St-Hil) Ravena        | Quercetin, ruthin, kaferol, gallic acid, chlorogenic acid, elagic acid, caffeic acid | *C. albicans* | 0.2        | [66, 67]|

Candida Albicans
| Herbs                                | Active compounds                                                                 | Microorganism            | MIC: μg/mL | Ref.        |
|--------------------------------------|----------------------------------------------------------------------------------|--------------------------|------------|-------------|
| *Centaurium erythrae* Rafn            | Erytaurin, gentiopicrin, erytro-centaurin                                        | *C. albicans*,           | 10.5       | [49, 68]    |
| *Coriandrum sativum* L.              | Decanal, trans-2-decenal, 2-decen-1-ol, cyclodecane, mono- and sesquiterpene     | *C. albicans*            | 0.007      | [60, 92, 122]|
|                                      | hydrocarbons                                                                      | *C. tropicalis*,        | 20         |             |
|                                      |                                                                                  | *C. stellatoidea*       | 32         |             |
|                                      |                                                                                  | *C. krusei*             | 20         |             |
| *Chrysobalanus icaco*                | Pomolic acid                                                                      | *C. albicans*,          | 1.56       | [71]        |
|                                      |                                                                                  | *C. tropicalis*         | 6.25       |             |
| *Croton campestris* L.               | Spathulenol, borneol, B-caryophyllene, 1,8-cineole                                 | *C. albicans*           | 5.25       | [49, 123, 124]|
| *Curatella americana* L.             | Tannins, 4-O-methyl—catechin; epicatechin-3-O-gallate; 4-O-methyl-catechin-3-O-gallate | *C. albicans*           | 15.6       | [73]        |
|                                      |                                                                                  | *C. tropicalis*         | 31.3       |             |
|                                      |                                                                                  | *C. parapsilosis*       | 31.3       |             |
| *Dalbergia ecastaphyllum*            | Luteolin, quercetin, biochanin A, Dalbergin, liquiritigenin, rutin                 | *C. albicans*,          | 64         | [125, 126]  |
| *Drimys winteri*                     | Polygodial, caffeic acid, 3-cafeoylquinic acid                                    | *C. albicans*           | 0.015      | [92, 127]   |
| *Eugenia dysenterica* ex DC Mart.    | Caryophyllene, bicyclogermacrene, spathulenol, Caryophyllene oxide                | *C. albicans*,          | 20         | [69, 92]    |
|                                      |                                                                                  | *C. tropicalis*,        | 32         |             |
|                                      |                                                                                  | *C. stellatoidea*       | 32         |             |
|                                      |                                                                                  | *C. krusei*             | 20         |             |
|                                      |                                                                                  | *C. albicans*           | 0.250      |             |
| *Eugenia uniflora* Linn              | Castor oil, isoquercetin, quercetin                                              | *C. krusei*             | 250        | [79, 80, 128]|
|                                      |                                                                                  | *C. famata*             | 125        |             |
|                                      |                                                                                  | *C. guilliermondii*     | 500        |             |
|                                      |                                                                                  | *C. tropicalis*         | 125        |             |
| *Equisetum arvense* L.               | Camptothin A, Eugilfors D1 and D2, afzelin, myricitrin, quercetin, myricitin,     | *C. albicans*           | 0.250      | [129, 81, 82, 130]|
|                                      | betulinic acid, centelloside C                                                  | *C. tropicalis*        | 1000       |             |
|                                      |                                                                                  | *C. krusei*             | 31.2       |             |
|                                      |                                                                                  | *C. parapsilosis*       | 125        |             |
| *Glycyrrhiza glabra* L.              | Flavonoids, phenolic acids, alkaloids, phytosterols, tannins, and triterpenoids  | *C. albicans*           | 0.78–3.12  | [131, 132]  |
| Herbs                         | Active compounds                                                                 | Microorganism | MIC: μg/mL | Ref.  |
|-------------------------------|----------------------------------------------------------------------------------|---------------|------------|-------|
| *Hymenaea courbaril* L.       | Triterpenic saponins, glycyrrhizin, glabridin                                    | *C. glabrata* | 8          | [133] |
| *Jacaranda cuspidifolia* Mart.| Terpene, phenolic, salicylic acid                                               | *C. albicans* | 1.25       | [87]  |
| *Jacaranda cuspidifolia* Mart. | Terpene, phenolic, salicylic acid                                               | *C. glabrata* | 0.625      |       |
| *Jacaranda cuspidifolia* Mart. | Terpene, phenolic, salicylic acid                                               | *C. kruisei*  | 1.25       |       |
| *Lafoensia pacari* St. Hil.   | Saponins, coumarins, quinones, flavonoids, tannins, triterpenes, steroids, alkaloids | *C. albicans* | 16         | [90]  |
| *Lippia sidoides* Cham.       | Ellagic acid                                                                     | *C. albicans* | 4.40       | [60, 92]|
| *Malva sylvestris* L.         | Isoborneol, bornyl acetate, α-humulene, α-fenchene                               | *C. albicans* | 0.250      | [92, 134]|
| *Maytenus salicifolia* Mart Ex Reiss | Mucopolysaccharides, mucilages, flavonoids                                       | *C. albicans* | 20         | [69, 93, 94]|
| *Maytenus salicifolia* Mart Ex Reiss | Mucopolysaccharides, mucilages, flavonoids                                       | *C. tropicalis* | 32         |       |
| *Maytenus salicifolia* Mart Ex Reiss | Mucopolysaccharides, mucilages, flavonoids                                       | *C. stellatoidea* | 32         |       |
| *Maytenus salicifolia* Mart Ex Reiss | Mucopolysaccharides, mucilages, flavonoids                                       | *C. kruisei*  | 20         |       |
| *Melaleuca alternifolia* Cheel | Tannins, nepeticin, rigidenol, gliquidone, 11-Î±-hydroxygliquidone, 16-b-hydroxypristymerin | *C. albicans* | 50         | [95, 96]|
| *Mentha piperita* L.          | 8-cineole, neomenthol, menthol, carvone, acetato de metila, transcariofileno e viridiflorol menthol, menthone | *C. albicans* | 0.73       | [87, 97, 98]|
| *Myroxylon peruiferum*         | α-Copaene, safrole, δ-cadinene, cumarin, cabreuvinia                             | *C. albicans* | 0.500      | [55, 92]|
| *Psidium guajava*             | Phenolic, flavonoid, carotenoid, terpenoid triterpene                            | *C. albicans* | 1.25       | [87, 99, 135]|
| *Psidium guajava*             | Phenolic, flavonoid, carotenoid, terpenoid triterpene                            | *C. glabrata* | 1.25 μg    |       |
| *Psidium guajava*             | Phenolic, flavonoid, carotenoid, terpenoid triterpene                            | *C. kruisei*  | 0.625      |       |
| *Psidium guajava*             | Phenolic, flavonoid, carotenoid, terpenoid triterpene                            | *C. parapsilosis* | 0.625 |       |
| *Psidium guajava*             | Phenolic, flavonoid, carotenoid, terpenoid triterpene                            | *C. tropicalis* | 1.25      |       |
| *Punica granatum*             | Tannins, piperidine alkaloids, polyphenols, oxalic acid, malic acid, ascorbic acid, estrone punicic acid, punicalagin | *C. albicans* | 20         | [136, 69, 81]|
| *Punica granatum*             | Tannins, piperidine alkaloids, polyphenols, oxalic acid, malic acid, ascorbic acid, estrone punicic acid, punicalagin | *C. tropicalis* | 32         |       |
| *Punica granatum*             | Tannins, piperidine alkaloids, polyphenols, oxalic acid, malic acid, ascorbic acid, estrone punicic acid, punicalagin | *C. stellatoidea* | 20         |       |
| *Punica granatum*             | Tannins, piperidine alkaloids, polyphenols, oxalic acid, malic acid, ascorbic acid, estrone punicic acid, punicalagin | *C. kruisei*  | 32         |       |
| *Punica granatum*             | Tannins, piperidine alkaloids, polyphenols, oxalic acid, malic acid, ascorbic acid, estrone punicic acid, punicalagin | *C. albicans* | 125        |       |
| *Punica granatum*             | Tannins, piperidine alkaloids, polyphenols, oxalic acid, malic acid, ascorbic acid, estrone punicic acid, punicalagin | *C. kruisei*  | 15.6       |       |
There are few clinical studies in humans on the efficacy of extracts from Brazilian plants in the treatment of oral candidiasis. More recently, human effectiveness of Brazilian green propolis derived from *B. dracunculifolia* on plaque control and gingivitis [49] has been shown.
for the prevention and control of oral mucositis and candidiasis [147, 148] and compared green propolis gel with benzydamine hydrochloride in cancer patients and irradiated in the head and neck regions [149]. Also, the Brazilian red propolis, derived from *D. ecastaphyllum*, both extract and gel, inhibited *C. albicans* in vitro, periodontopathogenic bacteria in vitro and in vivo, besides controlling periodontitis in rats [150]. The antifungal activity of Brazilian green propolis, originated by *Baccharis dracunculifolia*, was proven when tested against *Candida albicans* collected from HIV-patients mouth. The authors also demonstrated the more effectiveness of propolis compared with usual antifungal tested [29].

4. Conclusions

In this chapter, there is information about the most used Brazilian species of plants against *Candida* species. The highest antimicrobial activities were obtained with diverse plant extracts. Some tests were done with the wild-type microorganisms collected from patients’ mouths; however, most tests were done using standardized American Type Culture Collection (ATCC) samples. There is a certain difficulty in doing clinical tests on humans, especially when it comes to natural products. On the other hand, tested are antibacterial and anticanical agents and could be used in the treatment of various oral diseases caused by multiresistant microbial agents. It is also clear from this study that the antifungal activity of these 38 medicinal plants was found with ethanolic, methanol, n-butanol, and chloroformic fractions. Studies have also revealed that the plants tested are not toxic at therapeutic doses with good antimicrobial properties. However, this study is an important step toward clinical evaluation in order to produce improved phytomedicine in the treatment of oral candidiasis for multiresistant *Candida albicans*.

Acknowledgements

The authors thank Ms. Lorena de Melo Santos for the English revision.

A. Plant image glossary index

Photo Credits (alphabetical order of Latin names): 1 Allium sativum, alho; 2 Anacardium humile, cajuzinho do campo. https://www.dicaparasude.com/beneficios-do-cajui/; 3 Anadenanthera colubrina (Vell.) Brenan; Angico branco. https://sites.unicentro.br/wp/manejoflorestal/8598-2/; 4 Annona sylvatica (Araticum) http://independente.com.br/os-araticuns/; 5 Arrabidea chica (crajirú), https://manausalerta.com.br/pesquisa-analisa-acao-anti-inflamatoria-do-crajiru/, 6 Azadirachta indica (nem) -https://br.pinterest.com/pin/520095456944307200/, 7 Baccharis dracunculifolia, alecrim. http://www.ufrgs.br/fitoecologia/florars/open_sp.php?img=14749, 8 Baccharis trimera (carqueja) - http://plantaslujan-a.blogspot.com/2015/01/baccharis-trimeras.html, 9 Calendula officinalis, calêndula. https://plantsam.com/calendula-officinalis/10 Ceiba
speciosa(https://www.ebay.co.uk/itm/50-seeds-of-CEiba-speciosa-Chorisia-speciosa-bottle-of-fake-kapok-tree-R-/151774995083, 11 Centaurium erythraea, centaurea. http://naturalhealingroom.com/Centaury-Herb-Centaurium-Erythraea_p_1337.html, 12 https://en.wikipedia.org/wiki/Chrysobalanus_iacao; 13 Coriandrum sativum, coentro. https://commons.wikimedia.org/wiki/File:Starr_070906-8875_Coriandrum_sativum.jpg; 14 Croton campestris, https://www.flickr.com/photos/142712970@N03/38936756240; 15 Curatella americana, cajueiro-bravo-do-campo. https://pt.wikipedia.org/wiki/Cajueiro-bravo-do-campo; 16 Dalbergia ecastophyllum http://www.ufal.edu.br/unidadeacademica/ceca/pt-br/pos-graduacao/zootecnia/dissertacoes/talita-almeida-de-paula; 17 Drimys winteri, https://futureforests.ie/products/drimys-winteri; 18 Equisetum arvense, https://www.ebay.com/itm/Equisetum-Arvense-15-Fresh-Seeds-Herb-Medicinal-Plant-Field-Common-Horsetail-/132339802749; 19 Eugenia dysenterica, cagaita. http://www.viveiroipe.com.br/?mudas=cagaita;20 Eugenia uniflora, pitangueira. https://www.fazfacil.com.br/jardim/pitangueira/; 21 Glycyrrhiza glabra https://www.indiamart.com/proddetail/glycyrrhiza-glabra-mulethi-extract-12502491912.html; 22 Hymenaea courbaril http://fredsonpaiareporter.blogspot.com/2017/01/hymenaea-courbaril-viveiro-da-patrulha.html; 23 Jacaranda cuspidifolia -https://br.pinterest.com/pin/24769866672935594/?lp=true; 26 Malva sylvestris, malva. http://johnstarnesurbanfarm.blogspot.com/2011/11/malva-sylvestris.
html; 27 *Maytenus salicifolia*, espinheira santa. [http://www.ervanariamarcosguiao.com/product-page/espinheira-santa](http://www.ervanariamarcosguiao.com/product-page/espinheira-santa); 28 Melaleuca alternifolia; 29 Mentha piperita, 30 Myroxylon peruiferum, 31 Psidium guajava, 32 Punica granatum, [http://www.medicinanatural.com.br](http://www.medicinanatural.com.br); 34 *Sapindus saponaria*, [https://www.flickr.com/photos/mercadanteweb/10829969066](https://www.flickr.com/photos/mercadanteweb/10829969066); 35 *Schinus therebintifolia*, [https://en.wikipedia.org/wiki/Schinus_terebinthifolia](https://en.wikipedia.org/wiki/Schinus_terebinthifolia); 36 *S. adstringens* [https://www.tudosobreplantas.com.br](https://www.tudosobreplantas.com.br); 37 *Vismia guianensis*, lacre. [http://tropical.theferns.info](http://tropical.theferns.info); 38 *Z. joazeiro* [http://www.naturezabela.com.br/2011/04/juazeiro-ziziphus-joazeiro.html](http://www.naturezabela.com.br/2011/04/juazeiro-ziziphus-joazeiro.html); 23 Photos of the author Vagner Rodrigues Santos: (1) *A. sativum*, (13) *Coriandrum sativum*, (24) *Lafoensia pacari*, (25) *Lippia sidoides*, (33) *Ricinus communis*.

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