# Medicinal Plants against Candida spp.

Subjects: Microbiology

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The use of natural products to promote health is as old as human civilization. In recent years, the perception of natural products derived from plants as abundant sources of biologically active compounds has driven their exploitation towards the search for new chemical products that can lead to further pharmaceutical formulations. Candida fungi, being opportunistic pathogens, increase their virulence by acquiring resistance to conventional antimicrobials, triggering diseases, especially in immunosuppressed hosts. They are also pointed to as the main pathogens responsible for most fungal infections of the oral cavity. This increased resistance to conventional synthetic antimicrobials has driven the search for new molecules present in plant extracts, which have been widely explored as alternative agents in the prevention and treatment of infections.

Keywords: Candida spp. ; oral disease ; oral biofilm ; infections ; medicinal plants ; plant extracts ; natural compounds ; antibiofilm strategies

## 1. Introduction

Medicinal plants have been used for several centuries to treat a wide variety of ailments. In recent years, the investigation into molecules derived from these plants, which play a fundamental role in the resistance of various pathogens, has boosted the study of their antibacterial and/or antibiofilm properties [1][2][3]. Some plant compounds can interact with bacterial proteins and cell membrane structures, damaging them and reducing their fluidity, while inhibiting their nucleic acid synthesis and interfering with the energy metabolism of the microorganisms themselves [2][4][5]. Additionally, the study of the antibiofilm properties associated with these molecules has revealed that, in addition to their fungicidal/bactericidal effect, other underlying mechanisms can lead to biofilm suppression, namely, disturbances at the level of bacterial regulation mechanisms [6].

The biofilm is a more resistant form of microbial existence on solid surfaces and air–liquid interfaces in which microorganisms multiply in a matrix of self-produced extracellular polymeric substances (EPS) [7]. Its resistance is directly related to the natural survival characteristics of the microbial cells that live in these communities. The slower growth of cells associated with the biofilm, as opposed to free-living microbial cells, and the tight regulation of the cellular processes, stand out, and are mainly caused by the more restricted contact of the cells inside the biofilm with external nutrients. In addition, the presence of an EPS matrix that hinders the action of antimicrobials contributes even more to the resistance of biofilms, since this matrix acts as a diffusion barrier against small molecules [8][9].

Biofilms can be found in a variety of surfaces, both biotic and abiotic. Particularly in the oral cavity, biofilm can be found in the teeth and mucosal surfaces and are thought to consist of approximately 700 bacterial species, 100 fungal species, and some viruses [10]. Since these microorganisms coexist in the same environment, there is the possibility of interactions between different species, a factor that can make an oral infection more difficult to treat, creating an environment of protection and tolerance for microorganisms against conventional antimicrobial agents [11].

One of the main groups of microorganisms that can be found in the normal oral flora is the genus *Candida*, which is composed of dimorphic commensal yeast. Although *Candida* species are mainly nonpathogenic, when an imbalance in the oral microbiome occurs, they are the main pathogens responsible for the occurrence of fungal infections in the oral cavity [12]. One of the key virulence factors associated with these microorganisms is their ability to adhere to oral surfaces and form biofilms, which function as a reservoir for this type of fungi, both in teeth and mucosal surfaces [13][14]. Several factors contribute to the unbalanced colonization and biofilm formation in the oral cavity by *Candida* spp., namely, low salivary flow, low pH and poor oral hygiene among others [15]. As an opportunistic pathogen, this yeast can also cause disease when the host's immune system is debilitated by the appearance of pathologies such as diabetes mellitus and Human Immunodeficiency Virus (HIV) infection, and by the use of broad-spectrum antibiotics, among others [16]. Additionally, as they are one of the largest acid producers in the oral cavity, *Candida* fungi can also be at the origin of dental caries through a localized infectious process [17][18][19].

Once the establishment of pathogenic oral biofilms occurs, the risk of the occurrence of systemic infections increases, as does the resistance of these infections to conventional antimicrobial therapies [20]. Currently, the treatment of *Candida* infections in the oral cavity is mostly done using broad-spectrum antimicrobials, however, conventional biocidal agents can cause substantial side effects if administered in high concentrations, including vomiting, diarrhea, mucosal desquamation, tooth discoloration, etc. [11][19]. Given the harmful effects of traditional antimicrobial agents, and the increasing microbial resistance to them, natural plant products have been pointed out as a safe and efficient alternative for the treatment of *Candida* infections in the oral cavity since, together with their anti-inflammatory, antioxidant, and analgesic properties, they also exert antimicrobial and antibiofilm effects over *Candida* spp [21].

## 2. The Bioactive Compounds of Plants

Folk knowledge about the medicinal use of plants has been transmitted for centuries [22]. In recent years, much of the ethnopharmaceutical research has been focused on more specific approaches in order to evaluate and understand the biological and pharmaceutical effects of medicinal and aromatic plants [22]. Plants are rich in a wide variety of secondary metabolites which play an important role in the defense against numerous pathogens. These molecules are also involved in adaptation to biotic and abiotic stresses, protection against ultraviolet radiation, oxidation of molecules, nutritional and water stresses, while performing functions at the tissue level structure, being able to add flavor and color to plant products [23].

Presently, about 200,000 different plant secondary metabolites have been isolated and identified [24]. They can be classified based on their chemical structures and/or biosynthetic pathways [25]. A simple classification includes three main groups: terpenoids (polymeric isoprene derivatives and biosynthesized from acetate via the mevalonic acid pathway), phenolics (biosynthesized from shikimate pathways, containing one or more hydroxylated aromatic ring), and alkaloids (nonprotein nitrogen-containing compounds, biosynthesized from amino acids, such as tyrosine) [26]. Terpenoids, the condensation products of C5 isoprene units, are the main components of plant volatiles and essential oils [27]. They present many important properties, including anti-insect, antimicrobial, antiviral, and antiherbivore properties [28]. Phenolic compounds are widely found in fruits, seeds, leaves, roots, and stems, and are known for their strong antioxidant ability and their anticancer, anti-inflammatory, hypolipidemic, and hypoglycemic properties [29][30]. They have at least one aromatic ring with one or more hydroxyl groups attached, ranging from low molecular weight molecules to large and complex ones [31]. Alkaloids are usually cyclic organic compounds that contain at least one nitrogen atom in an amine-type structure [32]. These compounds are known to possess varied biological activities such as antimicrobial and antimalarial properties, among others [33].

Many studies have been published regarding bioactive properties such as antioxidant [34][35], antitumoral [31][36], analgesic/anti-inflammatory [29][37], immunostimulant [38], antiseptic, and antimicrobial [39][40][41]. The antimicrobial and/or antibiofilm activity linked with some of these compounds is closely related to their ability to inhibit the synthesis of nucleic acids, disrupt the plasma membrane, inhibit efflux pumps, elicit mitochondrial disfunction, impair cell division and/or growth, and impair cell-wall formation, as shown in **Figure 1** [42][43].

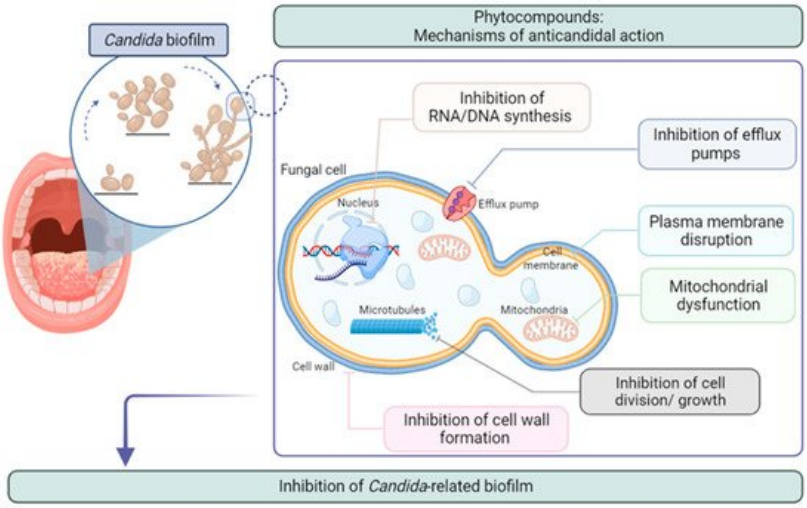


**Figure 1.** Mechanisms of action of phytocompounds against *Candida* spp. (Created with BioRender.com).

Given their strong bioactive potential, various types of phytocompounds are currently used in a wide range of fields such as food, pharmaceuticals, biomaterials, and environmental purification [44]. Regarding the ability of these compounds as antimicrobials, multiple studies have been conducted to determine their capability to fight oral infections caused by

opportunistic pathogens such as *Candida* species [45][46][47][48]. The increased virulence of some *Candida* species such as *Candida albicans* is largely related to their ability to form biofilms which, as mentioned before, makes oral infections caused by these microorganisms very difficult to treat [49]. Taking this information into account, the use of plant-derived products to fight oral pathologies caused by *Candida* appears as an alternative to conventional antifungal therapy. In oral care, the use of natural products to prevent candidiasis is receiving much attention and many studies have reported the effects of medicinal plant extracts on the inhibition of oral pathogen growth and inhibition of surfaces adhesion to surfaces [50]. Some of the most prescribed antimycotic agents that are currently used target the synthesis of fungal cell membrane components that are not found in human cells, such as ergosterol [51]. However, there are few available antifungal compounds that show low levels of cytotoxicity, given the similarities between human and fungal cells, making it urgent to search for and identify new molecules capable of disrupting biofilms formed by *Candida* spp. and increase the arsenal of antifungal agents [52][53]. Knowing this, screening plants as potential sources of molecules with antifungal and/or antibiofilm properties can be considered an excellent approach to combat the formation of *Candida* spp. oral biofilms and the establishment of infections [54].

## 3. Plant Extracts against Oral Biofilm Formed by *Candida* spp.

Most of the available antifungals are either ineffective against *Candida* biofilms or exhibit activity at very high concentrations [55]. Concerning microbial resistance, pharmacotherapy has reached its limit, threatening the effective prevention and treatment of an ever-increasing range of infections. These limitations have led to the search for novel molecules with antibiofilm potential. Plants are rich sources of bioactive molecules exhibiting various biological and pharmaceutical properties. Therefore, in recent years, new clinical approaches using natural phytocompounds have been the subject of several types of research, considering the composition of natural plant products in molecules with antimicrobial and/or antibiofilm potential. **Table 1** presents some of the plant species whose extracts hold compounds with antifungal/antibiofilm activity against *Candida* spp. Moreover, extracts able to inhibit biofilm formation and/or eradication in more than 99%, at concentrations ≤ 1 mg·mL$^{-1}$, were chosen for discussion.

*Allium sativum* L. (Amaryllidaceae) is an aromatic herbaceous annual plant, one of the oldest authenticated and most important herbs that have been used since ancient times in traditional medicine. It is one of the most described plant species with proven antifungal, antimicrobial, anti-aging, as well as anticancer properties, which have been confirmed by epidemiological data from human clinical studies [56]. This specie and its active components have been also reported to reduce the risk of diabetes and cardiovascular diseases [57][58]. *A. sativum* antibiofilm properties against oral cavity yeast were studied by Fahim et al. [59] who demonstrated that, for a concentration of 8.00 µg·mL$^{-1}$, *A. sativum* L. essential oil presented > 99.9% of growth reduction on biofilm of *C. albicans* ATCC 14053. The ability of this essential oil to inhibit biofilm formation seems to be correlated with its phenolic profile, with allicin, alliin and ajoene being the major compounds found in it [60].

Essential oils from some plants have shown high antifungal and/or antibiofilm activity against *Candida* species. An example of this are the species of *Cinnamomum cassia* (L.) J. Presl, *Cinnamomum zeylanicum* Blume, *Cymbopogon citratus* (DC.) Stapf, *Cymbopogon nardus* L. Rendle, and *Cymbopogon winterianus* Jowitt.

*C. cassia* (L.) J.Presl (Lauraceae), also known as “Chinese cinnamon,” is a well-known aromatic plant that has been widely cultivated and utilized to treat diabetes, ovarian cysts, stomach spasms, kidney disorders, high blood pressure, and menstrual disorders [61], and presents antimicrobial, antioxidant and antifungal properties [62]. *C. zeylanicum* Blume (Lauraceae) is an ever-green perennial plant that is used as a culinary herb [63]. This species presents several pharmacological properties such as antimicrobial, antioxidant, antifungal, and anticancer [64]. When it comes to oral health, a study performed by Almeida et al. [65] demonstrated that *C. cassia* essential oil, at a concentration of 1.00 mg·mL$^{-1}$, exerts more than 99.9% reduction in oral biofilm formation caused by *C. albicans* ATCC 90028, while *C. zeylanicum*, at a concentration of 1.6 µg·mL$^{-1}$, leads to more than 99.75% reduction in oral biofilm formation caused by *C. albicans* ATCC 10231. The high percentage of biofilm reduction shown by these two plants is attributed to the major phytocompound found in both species, the cinnamaldehyde. Cinnamaldehyde is a phenylpropanoid that may act on the cell membrane, likely binding to enzymes involved in the formation of the cytoplasmic membrane in fungal cells [66].

*C. citratus* (DC.) Stapf (Poaceae), commonly known as lemongrass, is an aromatic plant widely distributed around the world. It is used as a food flavouring, and is commonly consumed in teas and soups, but it may also be served with poultry, fish, beef, and seafood. Lemongrass essential oil exhibits a number of biological activities, including antioxidant [67], anti-inflammatory [68], antimicrobial [69], antifungal, and antibiofilm properties [70]. Almeida et al. [65] used the essential oil from *C. citratus* as an antifungal agent against *C. albicans* ATCC 10231 biofilms, and reported that, at the concentration of 6.4 µg·mL$^{-1}$, this essential oil was able to reduce the number of viable cells present in the biofilm by

99.79%. In this case, citral and neral were two of the main compounds found, which are known to hold antifungal properties [71][72].

*C. nardus* L. (Poaceae), popularly known as citronella, is a grass cultivated in subtropical and tropical regions of Asia, Africa, and America, including Brazil [73], The essential oil extracted from its leaves is commonly used in perfumes, the production of cosmetics, and as an insect repellent. Several studies have demonstrated the antiviral [74], antibacterial [75], and antifungal activities [76] of this oil. *C. winterianus* Jowitt (Poaceae) is an important aromatic plant cultivated in India and Brazil. In folk medicine, it is used for the treatment of anxiety, as a sedative, and for pain disorders [77]. Some studies demonstrated that the plant has anticonvulsant effects [78], anti-larvicidal effects against *Aedes aegypti* [79], and antibacterial and antifungal effects, including anti-*Candida* action [80]. The essential oils extracted from *C. nardus* L. and *C. winterianus* Jowitt species showed, in different studies, to be highly effective in combating *C. albicans* oral biofilms. *C. nardus* showed, at a concentration of 32.0 μg·mL$^{-1}$, an adherence inhibition of *C. albicans* ATCC 76645 higher than 99.0%, [81] and the application of *C. winterianus* essential oil, at a concentration of 1.00 mg·mL$^{-1}$, led to a reduction of *C. albicans* ATCC 90028 oral biofilm formation by more than 99.0%. In both species, the authors attributed the antibiofilm potential to the main compound identified in these species, namely citronellal. Citronellal is known to affect *C. albicans* cell growth by interfering with cell-cycle progression through the arrest of cells in S phase and affecting membrane integrity [82].

*Solidago virgaurea* L. (Asteraceae), commonly known as goldenrod, is a medicinal plant that is common throughout the world. In the literature, this plant is described as possessing a variety of medicinal properties such as antioxidant, anti-inflammatory, analgesic, spasmolytic, antihypertensive, antibacterial, antifungal and antitumor, among others [83]. Chevalier et al. [84] evaluated the effect of the extracts from two *S. virgaurea* subspecies, *S. virgaurea* subsp. *alpestris* and *S. virgaurea* subsp. *virgaurea*, on *C. albicans* oral biofilm growth. The results obtained showed that, at an extract concentration of 250 μg·mL$^{-1}$, *S. virgaurea* subsp. *alpestris* inhibition of oral biofilms from *C. albicans* IM003 was higher than 99.5%, and that *S. virgaurea* subsp. *virgaurea* inhibited the oral biofilm formation by *C. albicans* IM001 by more than 99.2%. Regarding the chemical composition of this plant, the compounds usually found in *S. virgaurea* are saponins, which have been attributed to the ability to inhibit the transition from yeast to hyphal growth [84]. This attribution seems reasonable considering the inherent surfactant properties of saponins, as well as their iron chelator qualities, iron being necessary for the growth and development of *Candida* spp. [85].

**Table 1.** Medicinal plants with antimicrobial/antibiofilm activity against oral *Candida* spp. and the respective bioactive compounds present in their extracts.

| Plant Name | Plant Extract | Compound | Microorganism | Results | | | | References |
|---|---|---|---|---|---|---|---|---|
| | | | | Antimicrobial Activity | | Antibiofilm Activity | | |
| ***Allium sativum* L.** | **Essential oil (bulbs)** | **Allicin, alliin, ajoene [60]** | ***C. albicans* ATCC 14053** | **MIC**<br>**IZD** | **8.0 μg·mL$^{-1}$**<br>**19.0 mm (50.0 μg·mL$^{-1}$)** | **>99.9% reduction** | **8.00 μg·mL$^{-1}$** | **[59]** |
| ***Aloysia gratissima* (Aff & Hook) Tronc.** | **Essential oil (leaves)** | ***(E)*-pinocamphone, β-pinene, guaiol** | ***C. albicans* CBS 562** | **MIC**<br>**MFC** | **0.015 mg·mL$^{-1}$**<br>**0.062 mg·mL$^{-1}$** | **12.3% inhibition** | **1.00 mg·mL$^{-1}$** | **[86]** |
| ***Artemisia judaica* L.** | **Essential oil (aerial plant parts)** | **Piperitone, camphor, ethyl cinnamate, chrysanthenone** | ***C. albicans* ATCC 10231** | **MIC** | **1.25 μg·mL$^{-1}$** | **50.0% reduction** | **2.5 μg·mL$^{-1}$** | **[87]** |

| Plant Name | Plant Extract | Compound | Microorganism | Results | | | | References |
|---|---|---|---|---|---|---|---|---|
| | | | | Antimicrobial Activity | | Antibiofilm Activity | | |
| *Brucea javanica* (L.) Merr. | Aqeuous extract (seeds) | Quassinoids, alkaloids, | *C. albicans* ATCC 14053 | | | 94.5% CSH reduction 79.7% adherence reduction | | [88] |
| | | | *C. dubliniensis* ATCC MYA-2975 | | | 90.4% CSH reduction 27.9% adherence reduction | | |
| | | | *C. glabrata* ATCC 90030 | | | 84.8% CSH reduction 76.8% adherence reduction | | |
| | | | *C. krusei* ATCC 14243 | | - | 97.0% CSH reduction 67.6% adherence reduction | 6.00 $mg{\cdot}mL^{-1}$ | |
| | | | *C. lusitaniae* ATCC 64125 | | | 91.1% CSH reduction 89.0% adherence reduction | | |
| | | | *C. parapsilosis* ATCC 22019 | | | 98.8% CSH reduction 49.0% adherence reduction | | |
| | | | *C. tropicalis* ATCC 13803 | | | 88.4% CSH reduction 89.9% adherence reduction | | |
| *Cassia spectabilis* DC. | Methanol extract (leaves) | (+)-spectaline; (−)-iso-6-cassine [89] | *C. albicans* 1 (CI) | MIC IZD | 6.25 $mg{\cdot}mL^{-1}$ 20 mm (100 $mg{\cdot}mL^{-1}$) | | | [90] |
| | | | *C. albicans* 2 (CI) | MIC IZD | 6.25 $mg{\cdot}mL^{-1}$ 21 mm (100 $mg{\cdot}mL^{-1}$) | 97% inhibition | 6.25 $mg{\cdot}mL^{-1}$ | |
| | | | *C. albicans* 3 (CI) | MIC IZD | 6.25 $mg{\cdot}mL^{-1}$ 23 mm (100 $mg{\cdot}mL^{-1}$) | | | |
| *Chenopodium ambrosioides* L. | Aqueous extract (leaves) | Kaempferol, quercetin | *C. albicans* ATCC 90028 | MIC<br>MFC | 0.250 $mg{\cdot}mL^{-1}$<br>0.250 $mg{\cdot}mL^{-1}$ | >99.0% reduction | 1.25 $mg{\cdot}mL^{-1}$ | [91] |

| Plant Name | Plant Extract | Compound | Microorganism | Results | | | | References |
|---|---|---|---|---|---|---|---|---|
| | | | | Antimicrobial Activity | | Antibiofilm Activity | | |
| *Cinnamomum cassia* L. J.Presl | Essential oil (leaves, bark, stalk) | Cinnamaldehyde, benzyl benzoate, α-pinene | *C. albicans* ATCC 90028 | MIC<br>MFC | 65.5 $\mu g \cdot mL^{-1}$ | >99.9% reduction | 1.00 $mg \cdot mL^{-1}$ | [65] |
| | | | *C. albicans* ATCC MYA-2876 | | | 50% reduction<br>50% inhibition | 0.15 $mg \cdot mL^{-1}$<br>1.0 $mg \cdot mL^{-1}$ | |
| *Cinnamomum verum* J.Presl | Essential oil (leaves) | Eugenol, benzyl benzoate, *trans*-caryophyllene, acetyle eugenol, linalool | *C. tropicalis* ATCC 750 | MIC | 1.0 $mg \cdot mL^{-1}$ | 50% reduction<br>50% inhibition | 0.35 $mg \cdot mL^{-1}$<br>>2.0 $mg \cdot mL^{-1}$ | [92] |
| | | | *C. dubliniensis* ATCC MYA-646 | | | 50% reduction<br>50% inhibition | 0.2 $mg \cdot mL^{-1}$<br>0.2 $mg \cdot mL^{-1}$ | |
| *Cinnamomum zeylanicum* Blume | Essential oil (leaves) | Cinnamaldehyde, cinnamyl acetate, cinnamyl benzoate [64] | *C. albicans* ATCC 10231 | MIC<br>MFC<br>IZD | 0.1 $\mu g \cdot mL^{-1}$<br>0.4 $\mu g \cdot mL^{-1}$<br>42.5 mm (50 $\mu g \cdot mL^{-1}$) | 99.75% reduction | 1.6 $\mu g \cdot mL^{-1}$ | [93] |
| | | | *C. albicans* CBS 562 | MIC<br>MFC | 15.6 $\mu g \cdot mL^{-1}$<br>31.2 $\mu g \cdot mL^{-1}$ | 53.43% inhibition | 62.50 $\mu g \cdot mL^{-1}$ | |
| | | | *C. tropicalis* CBS 94 | MIC<br>MFC | 31.2 $\mu g \cdot mL^{-1}$<br>62.5 $\mu g \cdot mL^{-1}$ | 89.76% inhibition | 125 $\mu g \cdot mL^{-1}$ | |
| *Coriandrum sativum* L. | Essential oil (leaves) | Decanal, *trans*-2-decenal, 2-decen-1-ol, cyclodecane, cis-2-dodecenal | *C. krusei* CBS 573 | MIC<br>MFC | 15.6 $\mu g \cdot mL^{-1}$<br>31.2 $\mu g \cdot mL^{-1}$ | 42.13% inhibition | 15.62 $\mu g \cdot mL^{-1}$ | [94] |
| | | | *C. dubliniensis* CBS 7987 | MIC<br>MFC | 31.2 $\mu g \cdot mL^{-1}$<br>62.5 $\mu g \cdot mL^{-1}$ | 61.51% inhibition | 62.50 $\mu g \cdot mL^{-1}$ | |
| | | | *C. rugosa* CBS 12 | MIC<br>MFC | 15.6 $\mu g \cdot mL^{-1}$<br>31.2 $\mu g \cdot mL^{-1}$ | 68.03% inhibition | 62.50 $\mu g \cdot mL^{-1}$ | |
| *Croton urucurana* Baill. | Methanol extract (stems) | (epi)-catechin dimer I [95] | *C. albicans* ATCC 10231 | | - | 46.0% inhibition | 0.500 $mg \cdot mL^{-1}$ | [96] |

| Plant Name | Plant Extract | Compound | Microorganism | Results | | | | References |
|---|---|---|---|---|---|---|---|---|
| | | | | Antimicrobial Activity | | Antibiofilm Activity | | |
| *Cymbopogon citratus* (DC.) Stapf | Essential oil (leaves) | Citral, neral, β-myrcene, geraniol [97] | *C. albicans* ATCC 10231 | MIC | 0.1 μL·mL$^{-1}$ | | | |
| | | | | MFC | 0.4 μL·mL$^{-1}$ | 99.79% reduction | 6.4 μL·mL$^{-1}$ | [93] |
| | | | | IZD | 18.2 mm (5% v.v$^{-1}$) | | | |
| | Ethanol extract (leaves) | Citral, geraniol, neral, camphene, limonene [98] | *C. albicans* ATCC 18804 | MIC | 0.625 mg·mL$^{-1}$ | >99.9% inhibition | 3.13 mg·mL$^{-1}$ | [99] |
| | | | | MFC | 2.50 mg·mL$^{-1}$ | 94.0% reduction | 6.25 mg·mL$^{-1}$ | |
| *Cymbopogon nardus* L. Rendle | Essential oil (leaves) | Citronellal, citronellol, geraniol | *C. albicans* ATCC 76645 | MIC<br>MFC | 32.0 μg·mL$^{-1}$ | >99.0% inhibition | 32.0 μg·mL$^{-1}$ | [100] |
| *Cymbopogon winterianus* Jowitt | Essential oil (leaves) | Citronellal, citronellol, geraniol | *C. albicans* ATCC 90028 | MIC<br>MFC | 250 μg·mL$^{-1}$ | >99.0% reduction | 1.00 mg·mL$^{-1}$ | [65] |
| *Cyperus articulatus* L. | Essential oil (bulbs) | α-pinene, mustakone, α-bulnesene | *C. albicans* CBS 562 | MIC | 0.125 mg·mL$^{-1}$ | 28.1% inhibition | 1.00 mg·mL$^{-1}$ | [99] |
| | | | | MFC | 0.500 mg·mL$^{-1}$ | | | |
| *Eucalyptus globulus* Labill. | Essential oil (leaves) | Hyperoside, quercitrin, myricetin [101] | *C. albicans* ATCC 14053 | | 0.219 mg·mL$^{-1}$ | 86% reduction | | [102] |
| | | | *C. tropicalis* ATCC 66029 | MFC | 0.885 mg·mL$^{-1}$ | 85% reduction | 22.5 mg·mL$^{-1}$ | |
| | | | *C. glabrata* ATCC 66032 | | 0.219 mg·mL$^{-1}$ | 85.2% reduction | | |
| *Houttuynia cordata* Thunb | Ethanol extract (leaves) | Aldehydes | *C. albicans* CAD1 | MFC | >2.17 mg·mL$^{-1}$ | 70.0% reduction | 1.00% (*v*/*v*) | [103] |
| *Lippia sidoides* Cham. | Essential oil (leaves) | Thymol, *p*-cymene, α-caryophyllene | *C. albicans* CBS 562 | MIC | 0.250 mg·mL$^{-1}$ | 16.5% inhibition | 1.00 mg·mL$^{-1}$ | [104] |
| | | | | MFC | 0.500 mg·mL$^{-1}$ | | | |
| *Melaleuca alternifolia* (Maiden & Betche) Cheel | Essential oil (leaves) | Terpinen-4-ol, *γ*-terpinene, *p*-cymene, *α*-terpinene,1,8-cineole, *α*-terpineol, *α*-pinene | *C. albicans* ATCC 18804 | MIC | 1.95 mg·mL$^{-1}$ | MBEC | 125 mg·mL$^{-1}$ | [105] |
| | Essential oil (leaves) | Terpinen-4-ol, *γ*-terpinene, *α*-terpinene, terpinolene, 1,8-cineole | *C. albicans* ATCC 10231 | MIC | 3.40 mg·mL$^{-1}$ | 131% adherence reduction | 0.75% (*v*/*v*) | [106] |
| | | | *C. albicans* SC5314 | MIC | 0.84 mg·mL$^{-1}$ | 76.0% adherence reduction | | |
| *Mikania glomerata* Spreng | Essential oil (leaves) | Germacrene D, α-caryophyllene, bicyclogermacrene | *C. albicans* CBS 562 | MIC | 0.250 mg·mL$^{-1}$ | 22.7% inhibition | 1.00 mg·mL$^{-1}$ | [104] |
| | | | | MFC | 0.250 mg·mL$^{-1}$ | | | |

| Plant Name | Plant Extract | Compound | Microorganism | Results | | | | References |
|---|---|---|---|---|---|---|---|---|
| | | | | Antimicrobial Activity | | Antibiofilm Activity | | |
| *Piper betle* L. | Aqueous extract (leaves) | Hydroxychavicol, cinnamoyl derivatives, luteolin, apigenin [107] | *C. albicans* ATCC 14053 | - | | 38.6% CSH reduction 61.4% adherence reduction | 6.00 $mg \cdot mL^{-1}$ | [88] |
| | | | *C. dubliniensis* ATCC MYA-2975 | | | 78.3% CSH reduction 21.4% adherence reduction | | |
| | | | *C. glabrata* ATCC 90030 | | | 71.4% CSH reduction 12.4% adherence reduction | | |
| | | | *C. krusei* ATCC 14243 | | | 31.6% CSH reduction 56.4% adherence reduction | | |
| | | | *C. lusitaniae* ATCC 64125 | | | 67.5% CSH reduction 47.6% adherence reduction | | |
| | | | *C. parapsilosis* ATCC 22019 | | | 48.1% CSH reduction 46.5% adherence reduction | | |
| | | | *C. tropicalis* ATCC 13803 | | | 29.7% CSH reduction 86.9% adherence reduction | | |
| *Rosmarinus officinalis* L. | Liposoluble extract (leaves) | Carnosic acid, carnosol [108] | *C. albicans* ATCC 18804 | MIC | 0.78 $mg \cdot mL^{-1}$ | 99.9% reduction | 200 $mg \cdot mL^{-1}$ | [109] |
| | | | | MMC | 3.13 $mg \cdot mL^{-1}$ | | | |

| Plant Name | Plant Extract | Compound | Microorganism | Results | | | References |
|---|---|---|---|---|---|---|---|
| | | | | Antimicrobial Activity | | Antibiofilm Activity | |
| *Satureja hortensis* L. | Essential oil (leaves and flowers) | Thymol, λ-terpinene, carvacrol, *p*-cymene | *C. albicans* F81 (CI) | MIC<br>MFC | 300 $\mu g \cdot mL^{-1}$<br>400 $\mu g \cdot mL^{-1}$ | 91.0% inhibition<br>91.0% reduction | [110] |
| | | | *C. albicans* F94 (CI) | | 200 $\mu g \cdot mL^{-1}$<br>300 $\mu g \cdot mL^{-1}$ | 90.0% inhibition<br>80.0% reduction | |
| | | | *C. albicans* F87 (CI) | | 300 $\mu g \cdot mL^{-1}$<br>400 $\mu g \cdot mL^{-1}$ | 86.0% inhibition<br>76.0% reduction | |
| | | | *C. albicans* F49 (CI) | | 400 $\mu g \cdot mL^{-1}$<br>600 $\mu g \cdot mL^{-1}$ | 92.0% inhibition<br>92.0% reduction | |
| | | | *C. albicans* F82 (CI) | | 400 $\mu g \cdot mL^{-1}$<br>600 $\mu g \cdot mL^{-1}$ | 89.0% inhibition<br>89.0% reduction | |
| | | | *C. albicans* F95 (CI) | | 400 $\mu g \cdot mL^{-1}$ | 81.0% inhibition<br>81.0% reduction | |
| | | | *C. albicans* F92 (CI) | | 300 $\mu g \cdot mL^{-1}$<br>600 $\mu g \cdot mL^{-1}$ | 90.0% inhibition<br>90.0% reduction | |
| | | | *C. albicans* F60 (CI) | | 400 $\mu g \cdot mL^{-1}$<br>600 $\mu g \cdot mL^{-1}$ | 80.0% inhibition<br>80.0% reduction | 4.80 $mg \cdot mL^{-1}$ |
| | | | *C. albicans* F86 (CI) | | 200 $\mu g \cdot mL^{-1}$<br>300 $\mu g \cdot mL^{-1}$ | 87.0% inhibition<br>87.0% reduction | |
| | | | *C. albicans* F91 (CI) | | 300 $\mu g \cdot mL^{-1}$<br>400 $\mu g \cdot mL^{-1}$ | 83.0% inhibition<br>83.0% reduction | |
| | | | *C. albicans* F69 (CI) | | | 91.0% inhibition<br>80.0% reduction | |
| | | | *C. albicans* F1 (CI) | | 200 $\mu g \cdot mL^{-1}$ | 87.0% inhibition<br>79.0% reduction | |
| | | | *C. albicans* F34 (CI) | | 300 $\mu g \cdot mL^{-1}$ | 86.0% inhibition<br>91.0% reduction | |
| | | | *C. albicans* F19 (CI) | | | 90.0% inhibition<br>85.0% reduction | |
| | | | *C. albicans* F78 (CI) | | 400 $\mu g \cdot mL^{-1}$<br>600 $\mu g \cdot mL^{-1}$ | 84.0% inhibition<br>84.0% reduction | |

| Plant Name | Plant Extract | Compound | Microorganism | Results | | | | References |
|---|---|---|---|---|---|---|---|---|
| | | | | Antimicrobial Activity | | Antibiofilm Activity | | |
| *Schinus terebinthifolia* Raddi. | Methanol extract (leaves) | Phenolic compounds, anthraquinones, terpenoids, alkaloids | *C. albicans* ATCC 10231 | - | | 47.0% inhibition | 0.007 mg·mL$^{-1}$ | [96] |
| *Solidago virgaurea* subsp. *alpestris* Waldst. & Kit. ex Willd. | Aqueous extract (aerial plant parts) | Saponins | *C. albicans* ATCC 10231 | NA (IZD) | | 95.9% inhibition<br>92.4% reduction | 0.250 mg·mL$^{-1}$<br>0.750 mg·mL$^{-1}$ | [84] |
| | | | *C. albicans* IM001 (CI) | | | 96.0% inhibition<br>82.2% reduction | 0.250 mg·mL$^{-1}$<br>0.750 mg·mL$^{-1}$ | |
| | | | *C. albicans* IM003 (CI) | | | 99.5% inhibition<br>76.3% reduction | 0.250 mg·mL$^{-1}$<br>0.750 mg·mL$^{-1}$ | |
| | | | *C. albicans* IM007 (CI) | | | 95.1% inhibition<br>91.9% reduction | 0.250 mg·mL$^{-1}$<br>0.750 mg·mL$^{-1}$ | |
| *Solidago virgaurea* L. subsp. *virgaurea*. | Aqueous extract (aerial plant parts) | Saponins | *C. albicans* ATCC 10231 | NA (IZD) | | 98.4% inhibition<br>77.9% reduction | 0.250 mg·mL$^{-1}$<br>0.750 mg·mL$^{-1}$ | |
| | | | *C. albicans* IM001 (CI) | | | 99.2% inhibition<br>91.1% reduction | 0.250 mg·mL$^{-1}$<br>0.750 mg·mL$^{-1}$ | |
| | | | *C. albicans* IM003 (CI) | | | 97.3% inhibition<br>79.2% reduction | 0.250 mg·mL$^{-1}$<br>0.750 mg·mL$^{-1}$ | |
| | | | *C. albicans* IM007 (CI) | | | 96.5% inhibition<br>90.9% reduction | 0.250 mg·mL$^{-1}$<br>0.750 mg·mL$^{-1}$ | |
| *Terminalia catappa* L. | Ethanol extract (leaves) | Caffeic acid, quercitrin, kaempferol, gallic acid, chlorogenic acid, isoquercitrin [111] | *C. albicans* ATCC 90028 | MIC<br>MFC | 6.25 mg·mL$^{-1}$<br>12.5 mg·mL$^{-1}$ | >98.0% reduction | 62.5 mg·mL$^{-1}$ | [112] |
| | *n*-butanol fraction from ethanol extract (leaves) | | *C. albicans* ATCC 90028 | MIC<br>MFC | 250 µg·mL$^{-1}$ | >99.5% reduction | 2.50 mg·mL$^{-1}$ | [113] |
| | | | *C. glabrata* ATCC 2001 | MIC<br>MFC | 250 µg·mL$^{-1}$ | >99.0% reduction | 2.50 mg·mL$^{-1}$ | |
| *Trachyspermum ammi* (L.) Sprague | Aromatic water (aerial plant parts) | Thymol, carvacrol, carvotanacetone | *C. albicans* CBS1905 | - | - | 95.2% inhibition | 0.5% (*v*/*v*) | [114] |
| *Zataria multiflora* Boiss. | Aqueous extract (whole plant) | Thymol, hydroxyl benzoic acid, and cymene [115] | *C. albicans* PTCC-5027 | MIC | 1.50 mg·mL$^{-1}$ | 87% reduction | 25 mg·mL$^{-1}$ | [116] |
| | Ethanolic extract (whole plant) | | | MIC | 0.84 mg·mL$^{-1}$ | 97% reduction | | |

## References


1. Quideau, S.; Deffieux, D.; Douat-Casassus, C.; Pouységu, L. Plant polyphenols: Chemical properties, biological activities, and synthesis. Angew. Chem. Int. Ed. Engl. 2011, 50, 586–621.
2. Daglia, M. Polyphenols as antimicrobial agents. Curr. Opin. Biotechnol. 2012, 23, 174–181.
3. Slobodníková, L.; Fialová, S.; Rendeková, K.; Kováč, J.; Mučaji, P. Antibiofilm Activity of Plant Polyphenols. Molecules 2016, 21, 1717.
4. Gyawali, R.; Salam, A.I. Natural products as antimicrobial agents. Food Control 2014, 46, 412–429.
5. Cushnie, T.P.T.; Lamb, A.J. Recent advances in understanding the antibacterial properties of flavonoids. Int. J. Antimicrob. Agents 2011, 38, 99–107.
6. Silva, L.N.; Zimmer, K.R.; Macedo, A.J.; Trentin, D.S. Plant Natural Products Targeting Bacterial Virulence Factors. Chem. Rev. 2016, 116, 9162–9236.
7. Donlan, R.M.; Costerton, J.W. Biofilms: Survival Mechanisms of Clinically Relevant Microorganisms. Clin. Microbiol. Rev. 2002, 15, 167–193.
8. Hall-Stoodley, L.; Stoodley, P. Evolving concepts in biofilm infections. Cell. Microbiol. 2009, 11, 1034–1043.
9. Anderson, G.G.; O'Toole, G.A. Innate and Induced Resistance Mechanisms of Bacterial Biofilms. In Bacterial Biofilms; Romeo, T., Ed.; Springer: Berlin/Heidelberg, Germany, 2008; Volume 322, pp. 85–105.
10. Brown, J.; Johnston, W.; Delaney, C.; Short, B.; Butcher, M.; Young, T.; Butcher, J.; Riggio, M.; Culshaw, S.; Ramage, G. Polymicrobial oral biofilm models: Simplifying the complex. J. Med. Microbiol. 2019, 68, 1573–1584.
11. Abusrewil, S.; Alshanta, O.A.; Albashaireh, K.; Alqahtani, S.; Nile, C.J.; Scott, J.A.; McLean, W. Detection, treatment and prevention of endodontic biofilm infections: What's new in 2020? Crit. Rev. Microbiol. 2020, 46, 194–212.
12. Baumgardner, D.J. Oral Fungal Microbiota: To Thrush and Beyond. J. Patient. Cent. Res. Rev. 2019, 6, 252–261.
13. Awawdeh, L.; Jamleh, A.; Al Beitawi, M. The Antifungal Effect of Propolis Endodontic Irrigant with Three Other Irrigation Solutions in Presence and Absence of Smear Layer: An In Vitro Study. Iran. Edond. J. 2018, 13, 234–239.
14. Phumat, P.; Khongkhunthian, S.; Wanachantararak, P.; Okonogi, S. Comparative inhibitory effects of 4-allylpyrocatechol isolated from Piper betle on Streptococcus intermedius, Streptococcus mutans, and Candida albicans. Arch. Oral Biol. 2020, 113, 104690.
15. Pfaller, M.A.; Diekema, D.J. Epidemiology of invasive candidiasis: A persistent public health problem. Clin. Microbiol. Rev. 2007, 20, 133–163.
16. Panda, A.K.; Barik, B.P. Review: Endodontic Bacterial Characterization. J. Int. Clin. Dent. Res. Organ. 2020, 12, 110–114.
17. Zhang, C.; Kuang, X.; Zhou, Y.; Peng, X.; Guo, Q.; Yang, T.; Zhou, X.; Luo, Y.; Xu, X. A Novel Small Molecule, ZY354, Inhibits Dental Caries-Associated Oral Biofilms. Antimicrob. Agents Chemother. 2019, 63, e02414–e02418.
18. Wu, J.; Fan, Y.; Wang, X.; Jiang, X.; Zou, J.; Huang, R. Effects of the natural compound, oxyresveratrol, on the growth of Streptococcus mutans, and on biofilm formation, acid production, and virulence gene expression. Eur. J. Oral Sci. 2020, 128, 18–26.
19. Chen, X.; Daliri, E.B.; Kim, N.; Kim, J.R.; Yoo, D.; Oh, D.H. Microbial Etiology and Prevention of Dental Caries: Exploiting Natural Products to Inhibit Cariogenic Biofilms. Pathogens 2020, 9, 569.
20. Galletti, J.; Tobaldini-Valerio, F.K.; Silva, S.; Kioshima, É.S.; Trierveiler-Pereira, L.; Bruschi, M.; Negri, M.; Estivalet Svidzinski, T.I. Antibiofilm activity of propolis extract on Fusarium species from onychomycosis. Future Microbiol. 2017, 12, 1311–1321.
21. Zida, A.; Bamba, S.; Yacouba, A.; Ouedraogo-Traore, R.; Guiguemdé, R.T. Anti-Candida albicans natural products, sources of new antifungal drugs: A review. J. Mycol. Med. 2017, 27, 1–19.
22. McClatchey, W.C.; Mahady, G.B.; Bennett, B.C.; Shiels, L.; Savo, V. Ethnobotany as a pharmacological research tool and recent developments in CNS-active natural products from ethnobotanical sources. Pharmacol. Ther. 2009, 123, 239–254.
23. Erb, M.; Kliebenstein, D.J. Plant Secondary Metabolites as Defenses, Regulators, and Primary Metabolites: The Blurred Functional Trichotomy. Plant. Physiol. 2020, 184, 39–52.
24. Kessler, A.; Kalske, A. Plant Secondary Metabolite Diversity and Species Interactions. Annu. Rev. Ecol. Evol. Syst. 2018, 49, 115–138.

25. Hussein, R.A.; El-anssary, A.A. Plants Secondary Metabolites: The Key Drivers of the Pharmacological Actions of Medicinal Plants. In Herbal Medicine; Builders, P.F., Ed.; IntechOpen: London, UK, 2019.

26. Gorlenko, C.L.; Kiselev, H.Y.; Budanova, E.V.; Zamyatnin, A.A., Jr.; Ikryannikova, L.N. Plant Secondary Metabolites in the Battle of Drugs and Drug-Resistant Bacteria: New Heroes or Worse Clones of Antibiotics? Antibiotics 2020, 9, 170.

27. Pichersky, E.; Jonathan, G. The formation and function of plant volatiles: Perfumes for pollinator attraction and defense. Curr. Opin. Plant Biol. 2002, 5, 237–243.

28. Franklin, L.U.; Cunnington, G.D.; Young, D. Terpene Based Pesticide Treatments for Killing Terrestrial Arthropods Including, Amongst Others, Lice, Lice Eggs, Mites and Ants. U.S. Patent US19990379268, 23 August 1999.

29. Rubió, L.; Motilva, M.J.; Romero, M.P. Recent advances in biologically active compounds in herbs and spices: A review of the most effective antioxidant and anti-inflammatory active principles. Crit. Rev. Food Sci. Nutr. 2013, 53, 943–953.

30. Alu'datt, M.H.; Rababah, T.; Alhamad, M.N.; Al-Rabadi, G.J.; Tranchant, C.C.; Almajwal, A.; Kubow, S.; Alli, I. Occurrence, types, properties and interactions of phenolic compounds with other food constituents in oil-bearing plants. Crit. Rev. Food Sci. Nutr. 2018, 58, 3209–3218.

31. Carocho, M.; Ferreira, I.C.F.R. The role of phenolic compounds in the fight against cancer—A review. Anticancer Agents Med. Chem. 2013, 13, 1236–1258.

32. The Editors of Encyclopaedia Britannica. Alkaloids. In Encyclopedia of Analytical Science, 2nd ed.; Worsfold, P., Townshend, A., Colin, P., Eds.; Elsevier: Oxford, UK, 2005; pp. 56–61.

33. Othman, L.; Sleiman, A.; Abdel-Massih, R.M. Antimicrobial Activity of Polyphenols and Alkaloids in Middle Eastern Plants. Front. Microbiol. 2019, 10, 911.

34. Roby, M.H.H.; Sarhan, M.A.; Selim, K.A.-H.; Khalel, K.I. Evaluation of antioxidant activity, total phenols and phenolic compounds in thyme (Thymus vulgaris L.), sage (Salvia officinalis L.), and marjoram (Origanum majorana L.) extracts. Ind. Crop. Prod. 2013, 43, 827–831.

35. Zielinski, A.; Haminiuki, C.; Alberti, A.; Nogueira, A.; Demiate, I.; Granato, D. A comparative study of the phenolic compounds and the in vitro antioxidant activity of different Brazilian teas using multivariate statistical techniques. Food Res. Int. 2014, 60, 246–254.

36. Zhao, J.G.; Yan, Q.Q.; Lu, L.Z.; Zhang, Y.Q. In vivo antioxidant, hypoglycemic, and anti-tumor activities of anthocyanin extracts from purple sweet potato. Nutr. Res. Pract. 2013, 7, 359–365.

37. Albishi, T.; John, J.; Al-Khalifa, A.; Shahidi, F. Antioxidant, anti-inflammatory and DNA scission inhibitory activities of phenolic compounds in selected onion and potato varieties. J. Funct. Foods 2013, 5, 930–939.

38. Bachiega, T.F.; de Sousa, J.P.B.; Bastos, J.K.; Sforcin, J.M. Clove and eugenol in noncytotoxic concentrations exert immunomodulatory/anti-inflammatory action on cytokine production by murine macrophages. J. Pharm. Pharmacol. 2012, 64, 610–616.

39. Sher, A. Antimicrobial Activity of Natural Products from Medicinal Plants. Gomal J. Med. Sci. 2004, 7, 72–78.

40. Mulaudzi, R.B.; Ndhlala, A.R.; Kulkarni, M.G.; Finnie, J.F.; Van Staden, J. Antimicrobial properties and phenolic contents of medicinal plants used by the Venda people for conditions related to venereal diseases. J. Ethnopharmacol. 2011, 135, 330–337.

41. Mangunwardoyo, W.; Deasywati; Usia, T. Antimicrobial and identification of active compound Curcuma xanthorrhiza Roxb. Int. J. Basic Appl. Sci. 2012, 12, 69–78.

42. Balasundram, N.; Sundram, K.; Samman, S. Phenolic compounds in plants and agri-industrial by-products: Antioxidant activity, occurrence, and potential uses. Food Chem. 2006, 99, 191–203.

43. Balange, A.K.; Benjakul, S. Effect of oxidised phenolic compounds on the gel property of mackerel (Rastrelliger kanagurta) surimi. LWT 2009, 42, 1059–1064.

44. Okumura, H. Application of phenolic compounds in plants for green chemical materials. Curr. Opin. Green Sustain. Chem. 2021, 27, 100418.

45. Alves, C.T.; Ferreira, I.C.F.R.; Barros, L.; Silva, S.; Azeredo, J.; Henriques, M. Antifungal activity of phenolic compounds identified in flowers from North Eastern Portugal against Candida species. Future Microbiol. 2014, 9, 139–146.

46. Martins, N.; Barros, L.; Henriques, M.; Silva, S.; Ferreira, I.C.F.R. In Vivo Anti-Candida Activity of Phenolic Extracts and Compounds: Future Perspectives Focusing on Effective Clinical Interventions. BioMed Res Int. 2015, 2015, 247382.

47. Khan, M.S.A.; Ahmad, I.B. Antibiofilm activity of certain phytocompounds and their synergy with fluconazole against Candida albicans biofilms. J. Antimicrob. Chemother. 2011, 67, 618–621.

48. Lu, M.; Li, T.; Wan, J.; Li, X.; Yuan, L.; Sun, S. Antifungal effects of phytocompounds on Candida species alone and in combination with fluconazole. Int. J. Antimicrob. Agents 2017, 49, 125–136.

49. Uppuluri, P.; Pierce, C.G.; López-Ribot, J.L. Candida albicans biofilm formation and its clinical consequences. Future Microbiol. 2009, 4, 1235–1237.

50. Cavalcanti, Y.W.; de Almeida, L.F.D.; Padilha, W.W.N. Anti-adherent activity of Rosmarinus officinalis essential oil on Candida albicans: An SEM analysis. Rev. Odonto Ciênc. 2011, 26, 139–144.

51. Onyewu, C.; Blankenship, J.R.; Del Poeta, M.; Heitman, J. Ergosterol Biosynthesis Inhibitors Become Fungicidal when Combined with Calcineurin Inhibitors against Candida albicans, Candida glabrata, and Candida krusei. Antimicrob. Agents Chemother. 2003, 47, 956–964.

52. Leroy, O.; Bailly, S.; Gangneux, J.P.; Mira, J.P.; Devos, P.; Dupont, H.; Montravers, P.; Perrigault, P.F.; Constantin, J.M.; Guillemot, D.; et al. Systemic antifungal therapy for proven or suspected invasive candidiasis: The AmarCAND 2 study. Ann. Intensive Care 2016, 6, 2.

53. Perfect, J.R. The antifungal pipeline: A reality check. Nat. Rev. Drug Discov. 2017, 16, 603–616.

54. Brighenti, F.L.; Salvador, M.J.; Gontijo, A.V.L.; Delbem, A.C.B.; Soares, C.P.; de Oliveira, M.A.C.; Girondi, C.M.; Yumi, K.-I.C. Plant extracts: Initial screening, identification of bioactive compounds and effect against Candida albicans biofilms. Future Microbiol. 2017, 12, 15–27.

55. Raut, J.S.; Karuppayil, S.M. Phytochemicals as Inhibitors of Candida Biofilm. Curr. Pharm. Des. 2016, 22, 4111–4134.

56. Batiha, G.E.S.; Beshbishy, A.M.; Wasef, L.G.; Elewa, Y.H.A.; Al-Sagan, A.A.; El-Hack, M.E.A.; Taha, A.E.; Abd-Elhakim, Y.M.; Devkota, H.P. Chemical Constituents and Pharmacological Activities of Garlic (Allium sativum L.): A Review. Nutrients 2020, 12, 872.

57. Li, Z.; Le, W.; Cui, Z. A novel therapeutic anticancer property of raw garlic extract via injection but not ingestion. Cell Death Discov. 2018, 4, 108.

58. Eidi, A.; Eidi, M.; Esmaeili, E. Antidiabetic effect of garlic (Allium sativum L.) in normal and streptozotocin-induced diabetic rats. Phytomedicine 2006, 13, 624–629.

59. Fahim, A.; Himratul-Aznita, W.H.; Abdul-Rahman, P.S. Allium-sativum and bakuchiol combination: A natural alternative to Chlorhexidine for oral infections? Pak. J. Med. Sci. 2020, 36, 271–275.

60. Martins, N.; Petropoulos, S.; Ferreira, I.C.F.R. Chemical composition and bioactive compounds of garlic (Allium sativum L.) as affected by pre- and post-harvest conditions: A review. Food Chem. 2016, 211, 41–50.

61. Silva, M.L.; Bernardo, A.; de Mesquita, M.F.; Singh, J. Beneficial Uses of Cinnamon in Health and Diseases: An Interdisciplinary Approach. In The Role of Functional Food Security in Global Health; Singh, R.B., Watson, R.R., Takahashi, T., Eds.; Academic Press-Elsevier: Amsterdam, The Netherlands, 2019; pp. 565–576.

62. Singh, A.; Deepika; Chaudhari, A.K.; Das, S.; Prasad, J.; Dwivedy, A.K.; Dubey, N.K. Efficacy of Cinnamomum cassia essential oil against food-borne molds and aflatoxin B1 contamination. Plant Biosyst. 2020, 155, 899–907.

63. Kiran, S.; Kujur, A.; Prakash, B. Assessment of preservative potential of Cinnamomum zeylanicum Blume essential oil against food borne molds, aflatoxin B1 synthesis, its functional properties and mode of action. Innov. Food. Sci. Emerg. Technol. 2016, 37, 184–191.

64. Boniface, Y.; Philippe, S.; Lima, H.; Pierre, N.; Alitonou, G.; Fatiou, T.; Sohounhloue, D. Chemical composition and Antimicrobial activities of Cinnamomum zeylanicum Blume dry Leaves essential oil against Food-borne Pathogens and Adulterated Microorganisms. Int. Res. J. Biol. Sci. 2012, 1, 18–25.

65. Almeida, L.F.D.; Paula, J.F.; Almeida, R.V.; Williams, D.W.; Hebling, J.; Cavalcanti, Y.W. Efficacy of citronella and cinnamon essential oils on Candida albicans biofilms. Acta Odontol. Scand. 2016, 74, 393–398.

66. da Nóbrega Alves, D.; Monteiro, A.F.M.; Andrade, P.N.; Lazarini, J.G.; Abílio, G.M.F.; Guerra, F.Q.S.; Scotti, M.T.; Scotti, L.; Rosalen, P.L.; Castro, R.D.; et al. Docking Prediction, Antifungal Activity, Anti-Biofilm Effects on Candida spp., and Toxicity against Human Cells of Cinnamaldehyde. Molecules 2020, 25, 5969.

67. Balakrishnan, B.; Paramasivam, S.; Arulkumar, A. Evaluation of the lemongrass plant (Cymbopogon citratus) extracted in different solvents for antioxidant and antibacterial activity against human pathogens. Asian Pac. J. Trop. Dis. 2014, 4, S134–S139.

68. Han, X.; Parker, T.L. Lemongrass (Cymbopogon flexuosus) essential oil demonstrated anti-inflammatory effect in pre-inflamed human dermal fibroblasts. Biochim. Open 2017, 4, 107–111.

69. Liakos, I.L.; D'autilia, F.; Garzoni, A.; Bonferoni, C.; Scarpellini, A.; Brunetti, V.; Carzino, R.; Bianchini, P.; Pompa, P.P.; Athanassiou, A. All natural cellulose acetate-Lemongrass essential oil antimicrobial nanocapsules. Int. J. Pharm. 2016, 510, 508–515.

70. Taweechaisupapong, S.; Ngaonee, P.; Patsuk, P.; Pitiphat, W.; Khunkitti, W. Antibiofilm activity and post antifungal effect of lemongrass oil on clinical Candida dubliniensis isolate. S. Afr. J. Bot. 2012, 78, 37–43.

71. Leite, M.C.A.; Bezerra, A.P.B.; de Sousa, J.P.; Guerra, F.Q.S.; Lima, E.O. Evaluation of Antifungal Activity and Mechanism of Action of Citral against Candida albicans. Evid. Based Complement. Alternat. Med. 2014, 2014, 378280.

72. Miron, D.; Battisti, F.; Silva, F.K.; Lana, A.D.; Pippi, B.; Casanova, B.; Gnoatto, S.; Fuentefria, A.; Mayorga, P.; Schapoval, E.E.S. Antifungal activity and mechanism of action of monoterpenes against dermatophytes and yeasts. Rev. Bras. Farmacogn. 2014, 24, 660–667.

73. Chen, Q.; Xu, S.; Wu, T.; Guo, J.; Sha, S.; Zheng, X.; Yu, T. Effect of citronella essential oil on the inhibition of postharvest Alternaria alternata in cherry tomato. J. Sci. Food Agric. 2014, 94, 2441–2447.

74. Aini, M.N.M.; Said, M.I.; Nazlina, I.; Hanina, M.N.; Ahmad, I.B. Screening for Antiviral Activity of Sweet Lemon Grass (Cymbopogon nardus (L.) Rendle) Fractions. J. Biol. Sci. 2006, 6, 507–510.

75. Innsan, M.F.M.F.; Shahril, M.H.; Samihah, M.S.; Asma, O.S.; Radzi, S.M.; Jalil, A.K.A.; Hanina, M.N. Pharmacodynamic properties of essential oils from Cymbopogon species. Afr. J. Pharm. Pharmacol. 2011, 5, 2676–2679.

76. Nakahara, K.; Alzoreky, N.; Yoshihashi, T.; Nguyen, T.; Trakoontivakorn, G. Chemical Composition and Antifungal Activity of Essential Oil from Cymbopogon nardus (Citronella Grass). Jpn. Agric. Res. Q. 2013, 37, 249–252.

77. Leite, B.L.S.; Bonfim, R.R.; Antoniolli, A.R.; Thomazzi, S.M.; Araújo, A.A.S.; Blank, A.F.; Estevam, C.S.; Cambui, E.V.F.; Bonjardim, L.R.; Albuquerque Jr, R.L.C.; et al. Assessment of antinociceptive, anti-inflammatory and antioxidant properties of Cymbopogon winterianus leaf essential oil. Pharm. Biol. 2010, 48, 1164–1169.

78. Quintans-Júnior, L.; Souza, T.; Leite, B.; Lessa, N.; Bonjardim, L.; Santos, M.; Alves, P.; Blank, A.; Antoniolli, A.R. Phytochemical screening and anticonvulsant activity of Cymbopogon winterianus Jowitt (Poaceae) leaf essential oil in rodents. Phytomedicine 2008, 15, 619–624.

79. Manh, H.D.; Hue, D.T.; Hieu, N.T.T.; Tuyen, D.T.T.; Tuyet, O.T. The Mosquito Larvicidal Activity of Essential Oils from Cymbopogon and Eucalyptus Species in Vietnam. Insects 2020, 11, 128.

80. Oliveira, W.; Pereira, F.; Luna, G.; Oliveira Lima, I.; Wanderley, P.; Lima, R.; Lima, E. Antifungal activity of Cymbopogon winterianus Jowitt ex bor against Candida albicans. Braz. J. Microbiol. 2011, 42, 433–441.

81. Costa, R.C.; Cavalcanti, Y.W.; Valença, A.M.G.; de Almeida, L.F.D. Sutures modified by incorporation of chlorhexidine and cinnamaldehyde: Anti-Candida effect, bioavailability and mechanical properties. Rev. Odontol. UNESP 2019, 48.

82. Zore, G.B.; Thakre, A.D.; Jadhav, S.; Karuppayil, S.M. Terpenoids inhibit Candida albicans growth by affecting membrane integrity and arrest of cell cycle. Phytomedicine 2011, 18, 1181–1190.

83. Cornelia, F.; Tatiana, C.; Livia, U.; Dinu, M.; Ancuceanu, R. Solidago virgaurea L.: A Review of Its Ethnomedicinal Uses, Phytochemistry, and Pharmacological Activities. Biomolecules 2020, 10, 1619.

84. Chevalier, M.; Medioni, E.; Prêcheur, I. Inhibition of Candida albicans yeast–hyphal transition and biofilm formation by Solidago virgaurea water extracts. J. Med. Microbiol. 2012, 61, 1016–1022.

85. Ashraf, M.F.; Abd Aziz, M.; Stanslas, J.; Ismail, I.; Kadir, M. Assessment of Antioxidant and Cytotoxicity Activities of Saponin and Crude Extracts of Chlorophytum borivilianum. Sci. World J. 2013, 2013, 216894.

86. Lavaee, F.; Moshaverinia, M.; Malek-Hosseini, S.; Jamshidzade, A.; Zarei, M.; Jafarian, H.; Haddadi, P.; Badiee, P. Antifungal effect of sesame medicinal herb on Candida Species: Original study and mini-review. Braz. J. Pharm. Sci. 2019, 55.

87. Abu-Darwish, M.S.; Cabral, C.; Gonçalves, M.; Cavaleiro, C.; Cruz, M.; Zulfiqar, A.; Khan, I.; Efferth, T.; Salgueiro, L. Chemical composition and biological activities of Artemisia judaica essential oil from southern desert of Jordan. J. Ethnopharmacol. 2016, 191, 161–168.

88. Nordin, M.A.; Wan Harun, W.H.; Abdul Razak, F. An in vitro study on the anti-adherence effect of Brucea javanica and Piper betle extracts towards oral Candida. Arch. Oral Biol. 2013, 58, 1335–1342.

89. Christofidis, I.; Welter, A.; Jadot, J. Spectaline and iso-6 cassine, two new piperidin 3-ol alkaloids from the leaves of cassia spectabilis. Tetrahedron 1977, 33, 977–979.

90. Torey, A.; Sasidharan, S. Anti-Candida albicans biofilm activity by Cassia spectabilis standardized methanol extract: An ultrastructural study. Eur. Rev. Med. Pharmacol. Sci. 2011, 15, 875–882.

91. Zago, P.M.W.; Dos Santos Castelo Branco, S.J.; de Albuquerque Bogea Fecury, L.; Carvalho, L.T.; Rocha, C.Q.; Madeira, P.L.B.; de Sousa, E.M.; de Siqueira, F.S.F.; Paschoal, M.A.B.; Diniz, R.S.; et al. Anti-biofilm Action of Chenopodium ambrosioides Extract, Cytotoxic Potential and Effects on Acrylic Denture Surface. Front. Microbiol. 2019, 10, 1724.

92. Wijesinghe, G.K.; Maia, F.C.; de Oliveira, T.R.; de Feiria, S.N.B.; Joia, F.; Barbosa, J.P.; Boni, G.C.; Sardi, J.C.O.; Rosalen, P.L.; Höfling, J.F. Effect of Cinnamomum verum leaf essential oil on virulence factors of Candida species and determination of the in vivo toxicity with Galleria mellonella model. Mem. Inst. Oswaldo Cruz 2020, 115, e200349.

93. Choonharuangdej, S.; Srithavaj, T.; Thummawanit, S. Fungicidal and inhibitory efficacy of cinnamon and lemongrass essential oils on Candida albicans biofilm established on acrylic resin: An in vitro study. J. Prosthet. Dent. 2021, 125, 707.e701–707.e706.

94. Freires, I.A.; Murata, R.M.; Furletti, V.F.; Sartoratto, A.; Alencar, S.; de Alencar, S.M.; Figueira, G.M.; de Oliveira Rodrigues, J.A.; Duarte, M.C.; Rosalen, P.L. Coriandrum sativum L. (Coriander) Essential Oil: Antifungal Activity and Mode of Action on Candida spp., and Molecular Targets Affected in Human Whole-Genome Expression. PLoS ONE 2014, 9, e099086.

95. Alves, J.J.; Inês, M.; Barreira, J.; Barros, L.; Resende, O.; Aguiar, A.; Ferreira, I.C.F.R. Phenolic Profile of Croton urucurana Baill. Leaves, Stems and Bark: Pairwise Influence of Drying Temperature and Extraction Solvent. Molecules 2020, 25, 2032.

96. Barbieri, D.S.; Tonial, F.; Lopez, P.V.; Sales Maia, B.H.; Santos, G.D.; Ribas, M.O.; Glienke, C.; Vicente, V.A. Antiadherent activity of Schinus terebinthifolius and Croton urucurana extracts on in vitro biofilm formation of Candida albicans and Streptococcus mutans. Arch. Oral Biol. 2014, 59, 887–896.

97. Ali, M.; Yusuf, M.; Nasraldeen Abdalaziz, M. GC-MS Analysis and Antimicrobial Screening of Essential Oil from Lemongrass (Cymbopogon citratus). Int. J. Pharm. Chem. 2017, 3, 72–76.

98. Majewska, E.; Kozłowska, M.; Gruczyńska-Sękowska, E.; Kowalska, D.; Tarnowska, K. Lemongrass (Cymbopogon citratus) Essential Oil: Extraction, Composition, Bioactivity and Uses for Food Preservation—A Review. Pol. J. Food Nutr. Sci. 2019, 69, 327–341.

99. Madeira, P.L.B.; Carvalho, L.T.; Paschoal, M.; de Sousa, E.M.; Moffa, E.; da Silva, M.A.S.; Tavarez, R.R.; Gonçalves, L. In vitro Effects of Lemongrass Extract on Candida albicans Biofilms, Human Cells Viability, and Denture Surface. Front. Cell. Infect. Microbiol. 2016, 6, 71.

100. Trindade, L.A.; de Araújo Oliveira, J.; de Castro, R.D.; de Oliveira Lima, E. Inhibition of adherence of C. albicans to dental implants and cover screws by Cymbopogon nardus essential oil and citronellal. Clin. Oral Investig. 2015, 19, 2223–2231.

101. Dezsi, Ș.; Bădărău, A.S.; Bischin, C.; Vodnar, D.C.; Silaghi-Dumitrescu, R.; Gheldiu, A.M.; Mocan, A.; Vlase, L. Antimicrobial and antioxidant activities and phenolic profile of Eucalyptus globulus Labill. and Corymbia ficifolia (F. Muell.) K.D. Hill & L.A.S. Johnson leaves. Molecules 2015, 20, 4720–4734.

102. Quatrin, P.M.; Verdi, C.M.; de Souza, M.E.; de Godoi, S.N.; Klein, B.; Gundel, A.; Wagner, R.; Vaucher, R.A.; Ourique, A.; Santos, R.C. Antimicrobial and antibiofilm activities of nanoemulsions containing Eucalyptus globulus oil against Pseudomonas aeruginosa and Candida spp. Microb. Pathog. 2017, 112, 230–242.

103. Sekita, Y.; Murakami, K.; Yumoto, H.; Amoh, T.; Fujiwara, N.; Ogata, S.; Matsuo, T.; Miyake, Y.; Kashiwada, Y. Preventive Effects of Houttuynia cordata Extract for Oral Infectious Diseases. BioMed Res. Int. 2016, 2016, 2581876.

104. Salete, M.F.B.; Galvo, L.C.C.; Goes, V.F.F.; Sartoratto, A.; Figueira, G.; Rehder, V.L.; Alencar, S.M.; Duarte, R.M.; Rosalen, P.L.; Duarte, M.C. Action of essential oils from Brazilian native and exotic medicinal species on oral biofilms. BMC Complement. Altern. Med. 2014, 14, 451.

105. Rasteiro, V.M.C.; da Costa, A.C.B.P.; Arajo, C.F.; de Barros, P.P.; Rossoni, R.D.; Anbinder, A.; Jorge, A.O.; Junqueira, J. Essential oil of Melaleuca alternifolia for the treatment of oral candidiasis induced in an immunosuppressed mouse model. BMC Complement. Altern. Med. 2014, 14, 489.

106. Tobouti, P.L.; Mussi, M.C.; Rossi, D.C.; Pigatti, F.M.; Taborda, C.P.; de Assis Taveira, L.A.; de Sousa, S.C. Influence of melaleuca and copaiba oils on Candida albicans adhesion. Gerodontology 2016, 33, 380–385.

107. Ferreres, F.; Oliveira, A.P.; Gil-Izquierdo, A.; Valentão, P.; Andrade, P.B. Piper betle leaves: Profiling phenolic compounds by HPLC/DAD-ESI/MS(n) and anti-cholinesterase activity. Phytochem. Anal. 2014, 25, 453–460.

108. Mena, P.; Cirlini, M.; Tassotti, M.; Herrlinger, K.A.; Dall'Asta, C.; Del Rio, D. Phytochemical Profiling of Flavonoids, Phenolic Acids, Terpenoids, and Volatile Fraction of a Rosemary (Rosmarinus officinalis L.) Extract. Molecules 2016, 21, 1576.

109. de Oliveira, J.R.; de Jesus, D.; Figueira, L.W.; de Oliveira, F.E.; Pacheco Soares, C.; Camargo, S.E.; Jorge, A.O.; de Oliveira, L.D. Biological activities of Rosmarinus officinalis L. (rosemary) extract as analyzed in microorganisms and cells. Exp. Biol. Med. 2017, 242, 625–634.

110. Sharifzadeh, A.; Khosravi, A.; Ahmadian, S. Chemical composition and antifungal activity of Satureja hortensis L. essentiall oil against planktonic and biofilm growth of Candida albicans isolates from buccal lesions of HIV(+)

individuals. Microb. Pathog. 2016, 96, 1–9.

111. Oyeleye, S.I.; Adebayo, A.A.; Ogunsuyi, O.B.; Dada, F.A.; Oboh, G. Phenolic profile and Enzyme Inhibitory activities of Almond (Terminalia catappa) leaf and Stem bark. Int. J. Food Prop. 2018, 20, S2810–S2821.
112. Machado-Gonçalves, L.; Tavares-Santos, A.; Santos-Costa, F.; Soares-Diniz, R.; Câmara-de-Carvalho-Galvão, L.; Martins-de-Sousa, E.; Beninni-Paschoal, M.A. Effects of Terminalia catappa Linn. Extract on Candida albicans biofilms developed on denture acrylic resin discs. J. Clin. Exp. Dent. 2018, 10, e642–e647.
113. Gonçalves, L.; Madeira, P.L.B.; Diniz, R.; Nonato, R.F.; de Siqueira, F.S.F.; de Sousa, E.M.; Farias, D.; Rocha, F.M.G.; Rocha, C.H.L.; Lago, A.D.N.; et al. Effect of Terminalia catappa Linn. on Biofilms of Candida albicans and Candida glabrata and on Changes in Color and Roughness of Acrylic Resin. J. Evid. Based Complement. Altern. Med. 2019, 2019, 7481341.
114. Arabi Monfared, A.; Ayatollahi Mousavi, S.A.; Zomorodian, K.; Mehrabani, D.; Iraji, A.; Moein, M.R. Trachyspermum ammi aromatic water: A traditional drink with considerable anti-Candida activity. Curr. Med. Mycol. 2020, 6, 1–8.
115. Shaiq Ali, M.; Saleem, M.; Ali, Z.; Ahmad, V.U. Chemistry of Zataria multiflora (Lamiaceae). Phytochemistry 2000, 55, 933–936.
116. Rahimi, G.; Khodavandi, A.; Janesar, R.; Alizadeh, F.; Yaghobi, R.; Sadri, F. Evaluation of Antifungal Effects of Ethanolic and Aqueous Extracts of Zataria Multiflora Herb in the Pathogenic Yeast Candida albicans Biofilm Inhibition. J. Pure Appl. Microbiol. 2014, 8, 4559–4564.