

Candida and anti-candidal plant compounds

Subjects: **Plant Sciences**

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Fungi from the genus *Candida* are very important human and animal pathogens. Many strains can produce biofilms, which inhibit the activity of antifungal drugs and increase the tolerance or resistance to them as well.

Candida

biofilm

treatment

antifungals

natural compounds

essential oil

extract

minimal inhibitory concentration (MIC)

1. Introduction

The genus *Candida* contains about 150 species; however, most are environmental organisms. The most medically important is *Candida albicans*, which accounts for about 80% of infections. *C. albicans* causes more than 400,000 cases of bloodstream life-threatening infections annually, with a mortality rate of about 42% ^[1]. *Candida* non-*albicans* species that are mainly responsible for infections are *C. glabrata*, *C. parapsilosis*, *C. tropicalis*, *C. krusei*, and *C. dubliniensis* ^[2]. Less frequently identified are *C. guilliermondii*, *C. lusitaniae*, *C. rugosa*, *C. orthopsilosis*, *C. metapsilosis*, *C. famata*, *C. inconspicua*, and *C. kefyr* ^[3].

C. albicans is a member of the commensal microflora. It colonizes the oral mucosal surface of 30–50% of healthy people. The rate of carriage increases with age and in persons with dental prostheses up to 60% ^{[4][5][6]}. Opportunistic infection caused by *Candida* species is termed candidiasis. At least one episode of vulvovaginal candidiasis (or thrush) concerns 50 to 75% of women of childbearing age ^[7]. Candidiasis can also affect the oral cavity, penis, skin, nails, cornea, and other parts of the body. In immunocompromised persons, untreated candidiasis poses the risk of systemic infection and fungemia ^{[5][8]}. *Candida* can be an important etiological factor in the infection of chronic wounds that are difficult to treat; this is mainly related to the production of biofilm ^[9].

Treatment of candidiasis depends on the infection site and the patient's condition. According to guidelines, vulvovaginal candidiasis should be treated with oral or topical fluconazole; however, regarding *C. glabrata* infection, topical boric acid, nystatin, or flucytosine is suggested. In oropharyngeal candidiasis, the treatment options include clotrimazole, miconazole, or nystatin, and in severe disease, fluconazole or voriconazole. In candidemia and invasive candidiasis, the drugs of choice are echinocandins (caspofungin, micafungin, anidulafungin), fluconazole, or voriconazole; in resistant strains, amphotericin B is used. In selected cases of candidemia caused by *C. krusei*, voriconazole is recommended ^{[10][11][12]}. More details can be found in the Guidelines of the Infectious Diseases Society of America ^[12] and the European Society of Clinical Microbiology and Infectious Diseases ^[11]. Increasingly, *Candida* species are becoming resistant to drugs. Marak and Dhanashree ^[13] tested the resistance of

90 *Candida* strains isolated from different clinical samples, such as pus, urine, blood, and body fluid. Their study revealed that about 41% of *C. albicans* strains are resistant to fluconazole and voriconazole. Simultaneously, about 41% of *C. tropicalis* strains are resistant to voriconazole and about 36% of strains to fluconazole. In strains of *C. krusei*, about 23% are resistant to fluconazole and about 18% to voriconazole. Rudramurthy et al. [14] studied resistance in *C. auris*, which is considered a multiresistant pathogen. Among 74 strains obtained from patients with candidemia, over 90% of strains were resistant to fluconazole and about 73% to voriconazole. Virulence factors of *Candida* species include the secretion of hydrolases, the transition of yeast to hyphae, phenotypic switching, and biofilm formation [15][16]. All microorganisms in biofilm form are more resistant to antimicrobial and host factors, which leads to difficulties in eradication [17]. It has also been shown that resistance to drugs increases significantly in the case of *Candida* biofilm occurrence. Biofilm prevents the spread of antifungals; moreover, fluconazole is bound by the biofilm matrix [18]. The formation of a *Candida* biofilm during infection increases mortality, length of hospital stay, and cost of antifungal therapy [19].

2. Plant Preparations That Display Activity against Candida Biofilms

The present review includes 60 articles in which *Candida* biofilm formation was inhibited by at least 50%. It has been shown that preparations from 34 plants demonstrate activity against *Candida* biofilms. Among them were 29 essential oils and 16 extracts. The plants from the following families dominated: Lamiaceae (6 species in 5 genera), Myrtaceae (5 species in 4 genera), Asteraceae (4 species in 4 genera), Fabaceae (4 species in 3 genera), and Apiaceae (4 species in 2 genera).

Plants from the Lamiaceae family had the best antifungal activity, including *Lavandula dentata* (0.045–0.07 mg/L) [20], *Satureja macrosiphon* (0.06–8 mg/L) [21], and *Ziziphora tenuior* (2.5 mg/L) [22]. *Artemisia judaica* (2.5 mg/L) from the Asteraceae family [23], *Lawsonia inermis* (2.5–12.5 mg/L) from the Lythraceae family [24], and *Thymus vulgaris* (12.5 mg/L) from the Lamiaceae family [25] likewise exhibited good antifungal activity (Table 1). All preparations were essential oils, with the exception of *Lawsonia inermis*, which was an extract. Most of the plant preparations presented in Table 1 acted on biofilm formation and/or mature biofilms.

Table 1. Antifungal (MICs) and anti-biofilm (inhibition >50%) activity of plant preparations (essential oils or extracts).

Name of Plant (Family)	Main Compounds Presented in the Reference (EO: Essential Oil)	Targeted Species of <i>Candida</i>	MICs (mg/L; mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L; mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
<i>Acorus calamus</i> var. <i>angustatus</i> Besser = A.	EO: asaraldehyde, 1-(2,4,5-	<i>C. albicans</i>	51.2	50–200	Mature biofilm;	[26]

Name of Plant (Family)	Main Compounds Presented in the Reference (EO: Essential Oil)	Targeted Species of <i>Candida</i>	MICs (mg/L; mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L; mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
<i>tatarinowii</i> Schott (Acoraceae)	trimethoxyphenyl)-1,2-propanediol, α-asarone, β-asarone, γ-asarone, acotatarone C				crystal violet and fluorescence microscopy	
<i>Allium sativum</i> L. (Amaryllidaceae)	Extract: allicin	<i>C. albicans</i>	400	60	Biofilm formation; XTT	[27]
<i>Aloysia gratissima</i> (Aff & Hook).Tr (Verbenaceae)	EO: E-pinocamphone (16.07%), β-pinene (12.01%), guaiol (8.53%), E-pinocarveol acetate (8.19%)	<i>C. albicans</i>	15	500	Biofilm formation; crystal violet	[28]
<i>Artemisia judaica</i> L. (Asteraceae)	EO: piperitone (30.4%), camphor (16.1%), ethyl cinnamate (11.0%), chrysanthenone (6.7%)	<i>C. albicans</i>	1.25	2.5	Mature biofilm; XTT	[23]
		<i>C. guilliermondii</i>	1.25	2.5		
		<i>C. krusei</i>	1.25	2.5		
		<i>C. parapsilosis</i>	1.25	2.5		
		<i>C. tropicalis</i>	1.25	2.5		
<i>Buchenavia tomentosa</i> Eichler (Combretaceae)	Extract: gallic acid, kaempferol, epicatechin, ellagic acid, vitexin, and corilagin	<i>C. albicans</i>	625	312.5	Biofilm formation and mature biofilm; culture	[29]
<i>Chamaecostus cuspidatus</i> (Nees & Mart.) C.Specht & D.W.Stev. (Costaceae)	Extract: dioscin, aferoside A, aferoside C	<i>C. albicans</i>	250	15.62	Biofilm formation and mature biofilm; MTT	[30]
<i>Cinnamomum verum</i> J. Presl (Lauraceae)	EO: eugenol (77.22%), benzyl benzoate (4.53%), <i>trans</i> -	<i>C. albicans</i>	1000	150	Biofilm adhesion; XTT	[31]
		<i>C. dubliniensis</i>	1000	200		

Name of Plant (Family)	Main Compounds Presented in the Reference (EO: Essential Oil)	Targeted Species of Candida	MICs (mg/L; mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L; mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
Citrus limon (L.) Osbeck (Rutaceae)	caryophyllene (3.39%), acetyl eugenol (2.75%), linalool 2.11%	C. tropicalis	1000	350	Biofilm formation and mature biofilm; XTT	[32]
		C. albicans	500	2000		
		C. glabrata	250	1000		
	EO: limonene (53.4%), neral (11%), geraniol (9%), trans-limonene oxide (7%), nerol (6%)	C. krusei	500	125		
		C. orthopsilosis	500	1000		
		C. parapsilosis	500	2000		
		C. tropicalis	250	2000		
Copaifera paupera (Herzog) Dwyer (Fabaceae)	Extract: galloylquinic acids, quercetrin, afzelin	C. glabrata	5.89	46.87	Biofilm formation and mature biofilm; XTT	[33]
Copaifera reticulata Ducke (Fabaceae)	Extract: galloylquinic acids, quercetrin, afzelin	C. glabrata	5.89	46.87	Biofilm formation and mature biofilm; XTT	[33]
Coriandrum sativum L. (Apiaceae)	EO: 1-decanol (33.91%), E-2-decen-1-ol (23.59%), 2-dodecen-1-ol (13.06%), E-2-tetradecen-1-ol (5.46%)	C. albicans	7	250	Biofilm formation; crystal violet	[28]
		C. albicans	15.6	62.5–125	Biofilm adhesion; crystal violet	[34]
	EO: decanal (19.09%), trans-2-decenal (17.54%), 2-decen-1-ol (12.33%), cyclodecane (12.15%)	C. dubliniensis	31.2	62.5–125		
		C. rugosa	15.6	62.5		

Name of Plant (Family)	Main Compounds Presented in the Reference (EO: Essential Oil)	Targeted Species of <i>Candida</i>	MICs (mg/L; mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L; mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
		<i>C. tropicalis</i>	31.2	31.25– 250		
<i>Croton eluteria</i> (L.) W.Wright (Euphorbiaceae)	EO: α-pinene (29.37%), β-pinene (19.35%), camphene (10.31%), 1,8-cineole (9.68%)	<i>C. albicans</i>	4000	5–500	Biofilm formation; confocal laser microscopy	[35]
		<i>C. albicans</i>	250	1000		
		<i>C. glabrata</i>	31.25	250		
<i>Cupressus sempervirens</i> L. (Cupressaceae)	EO: sabinene (20.3%), citral (20%), terpinene-4-ol (15.4%), α-pinene (8%)	<i>C. krusei</i>	62.5	62.5		
		<i>C. orthopsilosis</i>	31.25	125	Biofilm formation and mature biofilm; XTT	[32]
		<i>C. parapsilosis</i>	62.5	500		
		<i>C. tropicalis</i>	250	500		
<i>Cymbopogon citratius</i> (DC.) Stapf (Poaceae)	EO: no composition	<i>C. albicans</i>	180– 360	22.5– 180	Biofilm formation; XTT	[36]
<i>Cymbopogon martini</i> (Roxb.) W.Watson (Poaceae)	EO: no composition	<i>C. albicans</i>	16,800	800	Biofilm formation; XTT	[37]
<i>Cymbopogon nardus</i> (L.) Rendle (Poaceae)	EO: citronellal (27.87%), geraniol (22.77%), geranial (14.54%), citronellol (11.85%), neral (11.21%)	<i>C. albicans</i>	1000	2500– 5000		
		<i>C. krusei</i>	250– 500	2500	Biofilm adhesion; XTT	[38]
		<i>C. parapsilosis</i>	500– 1000	5000– 10,000		
<i>Cyperus articulatus</i> L. (Cyperaceae)	EO: α-pinene (5.72%), mustakone (5.66%), α-bulnesene	<i>C. albicans</i>	125	250	Biofilm formation; crystal violet	[28]

Name of Plant (Family)	Main Compounds Presented in the Reference (EO: Essential Oil)	Targeted Species of <i>Candida</i>	MICs (mg/L; mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L; mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
	(5.02%), α-copaene (4.97%)					
<i>Eucalyptus</i> sp. (Myrtaceae)	EO: no composition	<i>C. albicans</i>	8	8	Mature biofilm; luminescence	[39]
<i>Eucalyptus globulus</i> Labill. (Myrtaceae)	EO: 1,8-cineole (75.8%), p-cymene (7.5%), α-pinene (7.4%), limonene (6.4%)	<i>C. albicans</i>	219	11,250– 22,500	Mature biofilm; atomic force microscopy	[40]
		<i>C. glabrata</i>	219	11,250– 22,500		
		<i>C. tropicalis</i>	885	11,250– 22,500		
	EO: no composition	<i>C. albicans</i>	8400	500	Biofilm formation; XTT	[37]
<i>Eugenia brasiliensis</i> Lam. (Myrtaceae)	Extract: no composition	<i>C. albicans</i>	15.62– 31.25	156	Mature biofilm; scanning electron microscopy	[41]
<i>Eugenia leitonii</i> Legrand <i>nom. inval.</i> (Myrtaceae)	Extract: no composition	<i>C. albicans</i>	15.62– 250	156	Mature biofilm; scanning electron microscopy	[41]
<i>Helichrysum italicum</i> (Roth) G.Don (Asteraceae)	EO: α-pinene (27.64%), γ-elemene (23.84%), β- caryophyllene (13.05%), α- longipinene (11.25%)	<i>C. albicans</i>	6000	10–500	Biofilm formation; confocal laser microscopy	[35]
<i>Laserpitium latifolium</i> L. (Apiaceae)	Extract: laserpitine	<i>C. albicans</i>	1250	6300	Mature biofilm; luminescence	[42]
		<i>C. krusei</i>	1250	6300		

Name of Plant (Family)	Main Compounds Presented in the Reference (EO: Essential Oil)	Targeted Species of <i>Candida</i>	MICs (mg/L; mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L; mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
<i>Laserpitium ochridanum</i> Micevski (Apiaceae)	Extract: isomontanolide, montanolide, tarolide	<i>C. albicans</i>	5000	10,000	Mature biofilm; luminescence	[42]
		<i>C. krusei</i>	5000	10,000		
<i>Laserpitium zernyi</i> Hayek = <i>L. siler</i> subsp. <i>zernyi</i> (Hayek) Tutin (Apiaceae)	Extract: isomontanolide, montanolide, tarolide	<i>C. albicans</i>	7500	15,000	Mature biofilm; luminescence	[42]
		<i>C. krusei</i>	7500	37,500		
<i>Lavandula dentata</i> L. (Lamiaceae)	EO: eucalyptol (42.66%), β -pinene (8.59%), <i>trans</i> - α -bisabolene (6.34%), pinocarveol (6.3%)	<i>C. albicans</i>	0.15–0.18	0.045–0.07	Mature biofilm; XTT	[20]
<i>Lawsonia inermis</i> L. (Lythraceae)	Extract: no composition	<i>C. albicans</i>	10	2.5–12.5	Mature biofilm; MTT	[24]
<i>Lippia sidoides</i> Cham. (Verbenaceae)	EO: thymol (65.76%), p-cymene (17.28%), α -caryophyllene (10.46%), cyclohexanone (6.5%)	<i>C. albicans</i>	250	500	Biofilm formation; crystal violet	[28]
<i>Litsea cubeba</i> (Lour.) Pers. (Lauraceae)	EO: limonene (37%), neral (31.4%), citral (12%), linalool (4%)	<i>C. albicans</i>	500	2000	Biofilm formation and mature biofilm; XTT	[32]
		<i>C. glabrata</i>	250	2000		
		<i>C. krusei</i>	62.5	250		
		<i>C. orthopsilosis</i>	250	2000		
		<i>C. parapsilosis</i>	500	1000		
		<i>C. tropicalis</i>	1000	2000		
<i>Mentha</i> $\times$ <i>piperita</i> L. (Lamiaceae)	EO: menthol (32.93%), menthone (24.41%), 1,8-cineole (7.89%)	<i>C. albicans</i>	1–10	10	Biofilm formation; MTT	[43]

Name of Plant (Family)	Main Compounds Presented in the Reference (EO: Essential Oil)	Targeted Species of <i>Candida</i>	MICs (mg/L; mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L; mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
<i>Mikania glomerata</i> Spreng (Asteraceae)	EO: no composition	<i>C. albicans</i>	11,600	800	Biofilm formation; XTT	[37]
	EO: germacrene D (38.29%), α -caryophyllene (9.49%), bicyclogermacrene (7.98%), caryophyllene oxide (4.28%)	<i>C. albicans</i>	250	500	Biofilm formation; crystal violet	[28]
<i>Myrtus communis</i> L. (Myrtaceae)	EO: α -pinene (39.8%), 1,8-cineole (24.8%), limonene (10.7%), linalool (6.4%)	<i>C. albicans</i>	1250–10,000	None or 1250	No data; no data	[44]
		<i>C. parapsilosis</i>	1250 to >16,000	1250		
		<i>C. tropicalis</i>	1250–16,000	1250		
<i>Ononis spinosa</i> L. (Fabaceae)	Extract: kaempferol-O-dihexoside, kaempferol-O-hexoside-pentoside, kaempferol-O-hexoside, quercetin-O-hexoside-pentoside, acetylquercetin-O-hexoside	<i>C. albicans</i>	620	10,000	Mature biofilm; luminescence	[45]
		<i>C. krusei</i>	620	5000		
		<i>C. tropicalis</i>	310	10,000		
<i>Pelargonium graveolens</i> L'Hér. (Geraniaceae)	EO: geraniol (42.3%), linalool (20.1%), citronellol (11.1%), menthone (8.0%)	<i>C. albicans</i>	125	4000–8000	Mature biofilm; XTT	[46]
<i>Piper clausenianum</i> (Miq.) C. DC. (Piperaceae)	EO: nerolidols	<i>C. albicans</i>	4100–9600	2400–12,600	Mature biofilm; MTT	[47]

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1	Name of Plant (Family)	Main Compounds Presented in the Reference (EO: Essential Oil)	Targeted Species of <i>Candida</i>	MICs (mg/L; mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L; mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.	and, FL,
	<i>Portulaca oleracea</i> L. (Portulacaceae)	Extract: no composition	<i>C. albicans</i>	10	12.5	Mature biofilm; MTT	[24]	se of
	<i>Punica granatum</i> L. (Lythraceae)	Extract: ellagic acid	<i>C. albicans</i>	1000	100–750	Biofilm formation and mature biofilm; crystal violet	[48]	a
1	<i>Santolina impressa</i> Hoffmanns. & Link (Asteraceae)	EO: β-pinene (22.5%), 1,8-cineole (10.0%), limonene (9.1%), camphor (8.1%), β- phellandrene (8.0%)	<i>C. albicans</i>	540	70–1050	Biofilm formation; XTT	[49]	tance.
1	<i>Satureja hortensis</i> L. (Lamiaceae)	EO: thymol (45.9%), gamma-terpinen (16.71%), carvacrol (12.81%), p-cymene (9.61%)	<i>C. albicans</i>	200– 400	400– 4800	Biofilm adhesion, formation, and mature biofilm; MTT	[50]	or the Clin.
1	<i>Satureja macrosiphon</i> (Coss.) = <i>Micromeria macrosiphon</i> Coss. (Lamiaceae)	EO: linalool (28.46%), borneol (16.22%), terpinene-4-ol (14.58%), <i>cis</i> - sabinene hydrate (12.96%)	<i>C. albicans</i>	0.06–4	0.06–8	Biofilm formation; XTT	[21]	pp.
1			<i>C. dubliniensis</i>	0.25–4	2–8			
1	<i>Syzygium aromaticum</i> (L.) Merr. & L.M.Perry = <i>Eugenia caryophyllus</i> (Spreng.) Bullock & S.G.Harrison (Myrtaceae)	EO: no composition	<i>C. albicans</i>	100– 200	50	Biofilm formation; XTT	[36]	J.; analysis
1		EO: no composition	<i>C. albicans</i>	48,000	3300	Biofilm formation; XTT	[37]	2013, 4,
1	<i>Thymus vulgaris</i> L. (Lamiaceae)	EO: thymol (54.73%), carvacrol (12.42%), terpineol (4.00%), nerol acetate (2.86%), fenchol (0.5%)	<i>C. albicans</i>	1.56–25	12.5	Biofilm formation; absorbance, crystal violet, and scanning	[25]	against
1			<i>C. tropicalis</i>	25–50	12.5			nt, and

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1	Name of Plant (Family)	Main Compounds Presented in the Reference (EO: Essential Oil)	Targeted Species of Candida	MICs (mg/L; mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L; mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
2	Warburgia ugandensis Sprague (Canellaceae)	Extract: ugandential A, warburganal, polygodial, alpha-linolenic acid ALA	C. albicans	Lack of data	1000	electron microscopy	[51]
2			C. glabrata	Lack of data	1000	bioassay formation and mature biofilm; XTT and confocal laser microscopy	
2	Ziziphora tenuior L. (Lamiaceae)	EO: pulegone (46.8%), p-menth-3-en-8-ol (12.5%), isomenthone (6.6%), 8-hydroxymenthone (6.2%), isomenthol (4.7%)	C. albicans	1.25	2.5	Mature biofilm; XTT	[22]
2	Zuccagnia punctata L. (Fabaceae)	Extract: no composition	C. albicans	400	100	Biofilm formation and mature biofilm; XTT and crystal violet	[52]

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3. Plant Compounds That Display Activity against Candida Biofilm

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It has been shown that 69 compounds obtained from plants demonstrate activity against Candida biofilms (Table 2).

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Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
Antidesmone (alkaloid)	<i>Waltheria indica</i> , <i>W. brachypetala</i>	<i>C. albicans</i>	32	16	Mature biofilm; XTT	[55]
		<i>C. glabrata</i>	>32	16		
		<i>C. krusei</i>	16	16		
		<i>C. parapsilosis</i>	4	16		
		<i>C. tropicalis</i>	>32	16		
Anisaldehyde (phenolic aldehyde)	<i>Pimpinella anisum</i> , <i>Foeniculum vulgare</i>	<i>C. albicans</i>	500	500	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
Anisic acid (phenolic acid)	<i>Pimpinella anisum</i>	<i>C. albicans</i>	4000	4000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
Anisyl alcohol (phenolic alcohol)	<i>Pimpinella anisum</i>	<i>C. albicans</i>	31	500	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
Baicalein (flavonoid)	<i>Scutellaria baicalensis</i> , <i>S. lateriflora</i>	<i>C. albicans</i>	No data	4–32	Biofilm formation; XTT	[57]
Camphene (monoterpene)	<i>Croton eluteria</i> , <i>Cinnamomum verum</i>	<i>C. albicans</i>	No data	500	Biofilm formation; confocal laser microscopy	[35]
		<i>C. albicans</i>	1000	2000	Mature biofilm; XTT,	[58]

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Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
					crystal violet, and inverted light microscopy	[64]
Camphor (bicyclic monoterpene)	<i>Cinnamomum camphora</i> , <i>Artemisia annua</i>	<i>C. albicans</i>	125–250	Not or 62.5–250	Biofilm formation; crystal violet and absorbance	[59]
		<i>C. glabrata</i>	175	Not		
		<i>C. krusei</i>	350	Not		
		<i>C. parapsilosis</i>	125	Not		
		<i>C. tropicalis</i>	175	175		
Cannabidiol (cannabinoid)	<i>Cannabis sativa</i>	<i>C. albicans</i>	No data	12.5–100	Biofilm formation; confocal microscopy	[60]
Carvacrol (phenol)	<i>Thymus serpyllum</i> , <i>Carum carvi</i> , <i>Origanum vulgare</i>	<i>C. albicans</i>	250	500	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
			100–20,000	300–1250	Mature biofilm; XTT	[61]
			1000	750–1500	Biofilm formation; MTT	[62]
		<i>C. glabrata</i>	100–20,000	300–1250	Mature biofilm; XTT	[61]
		<i>C. parapsilosis</i>	100–20,000	300–1250		

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Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
Carvone/Limonene (monoterpene)	<i>Citrus × aurantium</i> , <i>Citrus limon</i>	<i>C. albicans</i>	1000	4000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
Carvone/Carvol (monoterpene)	<i>Carum carvi</i> , <i>Mentha spicata</i>	<i>C. albicans</i>	>4000	250	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
β-Caryophyllene (sesquiterpene)	<i>Helichrysum italicum</i> , <i>Caryophyllus aromaticus</i>	<i>C. albicans</i>	No data	100–500	Biofilm formation; confocal laser microscopy	[35]
1,4-Cineole (monoterpene)	<i>Rosmarinus officinalis</i> , <i>Thymus vulgaris</i>	<i>C. albicans</i>	>4000	4000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
1,8-Cineole/Eucalyptol (monoterpene)	<i>Eucalyptus globulus</i> , <i>Salvia officinalis</i> , <i>Pinus sylvestris</i>	<i>C. albicans</i>	4000	4000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
			8	4	Mature biofilm; luminescence	[39]
			3000–23,000	Not or 3000–23,000	Biofilm formation; crystal violet and absorbance	[59]
		<i>C. glabrata</i>	2000	Not	absorbance	

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Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
		<i>C. krusei</i>	4000	2000–4000		
		<i>C. parapsilosis</i>	2000	1000–2000		
		<i>C. tropicalis</i>	4000	2000–4000		
Cinnamaldehyde (aldehyde)	<i>Cinnamomum</i> sp., <i>Apium graveolens</i>	<i>C. albicans</i>	62	125	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
			50–400	25–200	Mature biofilm; XTT	[63]
Cinnamic acid (phenolic acid)	<i>Cinnamomum</i> sp.	<i>C. albicans</i>	2000	4000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
Citral (monoterpene)	<i>Melissa officinalis</i> , <i>Backhousia citriodora</i>	<i>C. albicans</i>	500	1000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
Citronellal (monoterpene)	<i>Cymbopogon citratus</i> , <i>Melissa officinalis</i>	<i>C. albicans</i>	500	1000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
β-Citronellol (monoterpene)	<i>Melissa officinalis</i> , <i>Pelargonium roseum</i>	<i>C. albicans</i>	500	1000	Mature biofilm; XTT, crystal violet, and inverted	[58]

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Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
					light microscopy	
Cuminaldehyde (monoterpene)	<i>Carum carvi</i> , <i>Cinnamomum verum</i>	<i>C. albicans</i>	1000 to >4000	6000–7000	Biofilm formation; MTT	[62]
p-Cymene (monoterpene)	<i>Thymus vulgaris</i> , <i>Eucalyptus</i> sp.	<i>C. albicans</i>	2000	4000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
8-Deoxoantidesmone (alkaloid)	<i>Waltheria indica</i>	<i>C. albicans</i>	16	32	Mature biofilm; XTT	[55]
		<i>C. glabrata</i>	>32	32		
		<i>C. krusei</i>	32	32		
		<i>C. parapsilosis</i>	32	32		
		<i>C. tropicalis</i>	>32	32		
2',4'-Dihydroxy-3'-methoxychalcone (chalcone)	<i>Zuccagnia punctata</i> , <i>Oxytropis falcata</i>	<i>C. albicans</i>	100	25	Biofilm formation and mature biofilm; XTT and crystal violet	[52]
Dioscin (steroidal saponin)	<i>Dioscorea</i> sp., <i>Chamaecostus</i>	<i>C. albicans</i>	3.9–15.62	3.9–31.25	Biofilm formation and mature biofilm; MTT	[30]
Ellagic acid (polyphenol)	<i>Punica granatum</i> L.	<i>C. albicans</i>	75–100	25–40	Biofilm formation and mature biofilm; crystal violet	[48]

Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
Emodin (anthraquinone)	<i>Rheum palmatum</i> , <i>Frangula alnus</i>	<i>C. albicans</i>	12.5–50	Not or 100–400	Biofilm adhesion; MTT	[64]
4α,5α-Epoxy-10α,14H-1-epi-inuviscolide (sesquiterpene lactone)	<i>Carpesium macrocephalum</i>	<i>C. albicans</i>	>128	38	Biofilm formation and mature biofilm; XTT	[65]
Eugenol (phenol)	<i>Syzygium aromaticum</i> , <i>Cinnamomum</i> sp.	<i>C. albicans</i>	50–400	12.5–200	Mature biofilm; XTT	[63]
			250	500	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
			500	500	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
			1200	10,000–80,000	Mature biofilm; XTT	[66]
			1000	500	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
Farnesol (sesquiterpene)	<i>Tilia</i> sp., <i>Cymbopogon</i> sp.	<i>C. albicans</i>	1000	500	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]

Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
Gallic acid (phenolic acid)	<i>Polygonum</i> sp., <i>Buchanavia tomentosa</i>	<i>C. albicans</i>	5000	2500	Biofilm formation and mature biofilm; culture	[29]
		<i>C. albicans</i>	1000	1000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
	<i>Pelargonium graveolens</i> , <i>Rosa</i> sp.	<i>C. albicans</i>	100–20,000	300–1250	Mature biofilm; XTT	[61]
		<i>C. albicans</i>	No data	1000–8000	Mature biofilm; XTT	[46]
		<i>C. glabrata</i>	100–20,000	300–1250	Mature biofilm; XTT	[61]
Geraniol (monoterpene)		<i>C. parapsilosis</i>	100–20,000	300–1250		
		<i>C. albicans</i>	500	1000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
		<i>C. albicans</i>	125–500	125–1000	Biofilm formation and mature biofilm; XTT	[67]
		<i>C. albicans</i>	250	250	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
		<i>C. albicans</i>				

Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
Isomontanolide (sesquiterpenic lactone)	<i>Laserpitium ochridanum</i> , <i>L. zernyi</i>	<i>C. albicans</i>	50	250	Mature biofilm; luminescence	[42]
		<i>C. krusei</i>	200	250		
Isopulegol (monotherpene)	<i>Mentha rotundifolia</i> , <i>Melissa officinalis</i>	<i>C. albicans</i>	>4000	250	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
Ivalin (sesquiterpene lactone)	<i>Geigeria aspera</i> , <i>Carpesium macrocephalum</i>	<i>C. albicans</i>	>128	15.4	Biofilm formation and mature biofilm; XTT	[65]
Laserpitine (sesquiterpene lactone)	<i>Laserpitium latifolium</i> , <i>Laserpitium halleri</i>	<i>C. albicans</i>	200	400	Mature biofilm; luminescence	[42]
		<i>C. krusei</i>	200	400		
Lichochalcone A (chalconoid)	<i>Glycyrrhiza</i> sp.	<i>C. albicans</i>	6.25–12.5	0.2–20	Biofilm formation; crystal violet	[68]
Linalool (monotherpene)	<i>Lavandula officinalis</i> , <i>Pelargonium graveolens</i>	<i>C. albicans</i>	No data	100–500	Biofilm formation; confocal laser microscopy	[35]
			2000	1000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
			No data	1000–8000	Mature biofilm; XTT	[46]
α-Longipinene (sesquiterpene)	<i>Croton eluteria</i> , <i>Helichrysum italicum</i>	<i>C. albicans</i>	No data	100–500	Biofilm formation; confocal	[35]

Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
					laser microscopy	
Menthol (monotherpene)	Mentha spp.	C. albicans	>4000	2000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
			2500	10,000–80,000	Mature biofilm; XTT	[66]
Montanolide (sesquiterpene lactone)	Laserpitium ochridanum, L. zernyi	C. albicans	200	400	Mature biofilm; luminescence	[42]
		C. krusei	200	400		
Morin (flavonoid)	Prunus dulcis , Morus alba	C. albicans	150	37.5–600	Biofilm formation; crystal violet	[69]
Myrcene (monotherpene)	Humulus lupulus, Cannabis sativa	C. albicans	1000	2000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
Nerol (monotherpene)	Citrus × aurantium, Humulus lupulus	C. albicans	2000	500	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
Nerolidols (sesquiterpene)	Citrus × aurantium, Piper claussonianum	C. albicans	18,600–62,500	2500–10,000	Mature biofilm; MTT	[47]
α-Pinene (monotherpene)	Pinus sylvestris, Picea abies	C. albicans	3125	3125	Biofilm formation; XTT	[70]
β-Pinene (monotherpene)	Pinus sylvestris, Picea abies	C. albicans	2000	4000	Mature biofilm; XTT,	[58]

Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
	[80]				crystal violet, and inverted light microscopy	
		[81]	187	187	Biofilm formation; XTT	[70]
compounds that inhibit (>50%) Candida biofilm formation are listed						
Polygodial (sesquiterpene)	[25] Warburgia ugandensis, Polygonum hydropiper [30] [63] [60]	[55] [72] [71] C. albicans	[57] 4.1	10.8	Biofilm formation and mature biofilm; XTT and confocal laser microscopy	[68] [51] [51]
		[65] C. glabrata	94.1	50.6–61.9		
Pterostilbene (polyphenol)	Pterocarpus marsupium, Pterocarpus santalinus, Vitis vinifera	C. albicans	No data	8–32	Biofilm formation and mature biofilm; XTT	[71]
Riccardin D (macrocyclic bisbibenzyl)	Dumortiera hirsuta	C. albicans	16	8–64	Mature biofilm; XTT	[72]
Salicylaldehyde (phenolic aldehyde)	Filipendula ulmaria, Fagopyrum esculentum	C. albicans	31	125	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
Salicylic acid (phenolic acid)	Salix sp., Filipendula ulmaria	C. albicans	4000	2000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
Scopoletin (cumarin)	Mitracarpus frigidus, Scopolia carniola	C. tropicalis	50	50	Biofilm adhesion, formation, and mature	[73]

Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
					biofilm; absorbance and digital scanning	
6-Shogaol (phenylalkane)	<i>Zingiber officinale</i>	<i>C. auris</i>	32–64	16–64	Mature biofilm; crystal violet	[74]
Tarolide (sesquiterpene lactone)	<i>Laserpitium ochridanum</i> , <i>L. zernyi</i>	<i>C. albicans</i>	400	1000	Mature biofilm; luminescence	[42]
		<i>C. krusei</i>	400	1000		
Telekin (sesquiterpene lactone)	<i>Carpesium macrocephalum</i> , <i>Telekia speciose</i>	<i>C. albicans</i>	>128	36	Biofilm formation and mature biofilm; XTT	[65]
Terpinolene (terpene)	<i>Cannabis sativa</i> , <i>Citrus limon</i>	<i>C. albicans</i>	2000	4000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
5,7,3',4'-Tetramethoxyflavone (flavonoid)	<i>Psiadia punctulate</i> , <i>Kaempferia parviflora</i>	<i>C. albicans</i>	100	40	Biofilm formation; crystal violet	[75]
α-Thujone (monoterpene)	<i>Artemisia absinthium</i> , <i>Tanacetum vulgare</i>	<i>C. albicans</i>	>4000	500	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
Thymol (phenol)	<i>Thymus vulgaris</i> , <i>Trachyspermum copticum</i>	<i>C. albicans</i>			Mature biofilm; XTT, crystal violet, and inverted light microscopy	[58]
			250	250		

Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
			1.56–50	3.12	Biofilm formation; absorbance, crystal violet, and scanning electron microscopy	[25]
			32–128	128	Biofilm adhesion and mature biofilm; XTT	[76]
			100–20,000	300–1250	Mature biofilm; XTT	[61]
			125	125–250	Biofilm formation and mature biofilm; XTT	[77]
			1200	5000–80,000	Mature biofilm; XTT	[66]
		<i>C. tropicalis</i>	1.56–50	12.5	Biofilm formation; absorbance, crystal violet, and scanning electron microscopy	[25]
		<i>C. glabrata</i>	100–20,000	300–1250	Mature biofilm; XTT	[61]
		<i>C. parapsilosis</i>	100–20,000	300–1250		
		<i>C. tropicalis</i>	32	16	Mature biofilm; XTT	[78]
		<i>C. albicans</i>	390	390	Biofilm formation and	[79]
Tn-AFP1 (protein)	<i>Trapa natans</i>					
5,6,8-Trihydroxy-7,4' dimethoxy flavone (flavonoid)	<i>Thymus membranaceus</i> subsp. <i>membranaceus</i> , <i>Dodonaea viscosa</i> var. <i>angustifolia</i>					

Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
					mature biofilm; MTT	
5(R)-Vanessine (alkaloid)	Waltheria indica	C. albicans	32	16	Mature biofilm; XTT	[55]
		C. glabrata	>32	16		
		C. krusei	32	16		
		C. parapsilosis	>32	16		
		C. tropicalis	>32	16		
Vanillic acid (phenolic acid)	Angelica sinensis , Solanum tuberosum	C. albicans	>4000	4000	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
Vanillin (phenol)	Vanilla planifolia	C. albicans	1000	500	Mature biofilm; XTT, crystal violet, and inverted light microscopy	[56]
Waltheriones (alkaloid)	Waltheria indica, W.viscosissima	C. albicans	4–32	8–32	Mature biofilm; XTT	[55]
		C. glabrata	32 or >32	8–32		
		C. krusei	16–32 or >32	8–32		
		C. parapsilosis	2–32 or >32	8–32		
		C. tropicalis	32 or >32	8–32		
Warburganal (sesquiterpene)	Warburgia sp.	C. albicans	4	4.5	Biofilm formation and	[51]

Active Compound	Example of Plant Origin	Targeted Fungus	MICs (mg/L, mL/L)	Inhibition of Biofilm Formation by at Least 50% (mg/L, mL/L)	Inhibited Stage of Biofilm; Method of Biofilm Detection	Ref.
		<i>C. glabrata</i>	72–72.6	49.1–55.9	mature biofilm; XTT and confocal laser microscopy	

Legend: MIC—minimal inhibitory concentration; XTT—reduction assay of 2,3-bis(2-methoxy-4-nitro-5-sulfophenyl)-5-[carbonyl(phenylamino)]-2H-tetrazolium hydroxide; MTT—reduction assay of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide [\[53\]](#)[\[54\]](#).