

Based on the provided sources, here are the natural compounds and herbs sorted by efficacy against *Candida* species (including multidrug-resistant strains like *C. auris* and *C. glabrata*).

## Tier 1: Superior Efficacy (Lethal at Low Doses & Anti-MDR)

### 1. Cinnamon Bark

- **Common Name:** Cinnamon.
- **Place of Origin:** Sri Lanka, Southeast Asia (specifically *Cinnamomum zeylanicum* and *C. cassia*).
- **Source:** Essential oil from the bark.
- **Commercial Production:** Yes, widely available globally.
- **Mechanism/Efficacy:** Rated as having the strongest antifungal activity among 21 tested oils against multidrug-resistant *Candida auris*. It demonstrated lethality (fungicidal activity) at concentrations lower than **0.01% (v/v)**, which was superior to many standard antifungal drugs in direct contact assays. It effectively destroys the fungal membrane structure.
- **Name:** *Cinnamomum verum* / *Cinnamomum zeylanicum*

### 2. Moroccan Thyme

- **Common Name:** Za-itra, Moroccan Thyme.
- **Place of Origin:** Endemic to Morocco (Tafraout region).
- **Source:** Essential oil from aerial parts (leaves/stems).
- **Commercial Production:** Yes, cultivable in North Africa.
- **Mechanism/Efficacy:** Demonstrated massive synergistic potential. When combined with the drug fluconazole, it reduced the required dosage of the drug by up to **512-fold** against resistant *Candida* strains. It contains high levels of carvacrol (78.75%), a potent membrane disruptor.
- **Name:** *Thymus leptobotrys*

### 3. Chinese Goldthread

- **Common Name:** Coptis, Huang Lian.
- **Place of Origin:** China (Traditional Chinese Medicine).
- **Source:** Decoction or essential oil from the rhizome (root).
- **Commercial Production:** Yes, widely cultivated for pharmaceutical use.
- **Mechanism/Efficacy:** Demonstrated broad-spectrum **fungicidal** activity (killing the yeast completely rather than just inhibiting growth) against *C. albicans*, *C. glabrata*, *C. krusei*, and *C. tropicalis*. It was effective against fluconazole-resistant strains with MIC values ranging from 0.63 to 5 µL/mL.
- **Name:** *Coptis chinensis*

#### **4. Clove**

- **Common Name:** Clove.
- **Place of Origin:** Indonesia (Maluku Islands).
- **Source:** Essential oil from the flower buds.
- **Commercial Production:** Yes, highly available.
- **Mechanism/Efficacy:** Displayed fungicidal activity at very low concentrations (0.06% to 0.13%) against *C. auris*. It showed synergistic activity when combined with fluconazole and flucytosine, significantly enhancing the killing effect against *C. albicans*, *C. glabrata*, and *C. tropicalis*.
- **Name:** *Syzygium aromaticum*

Tier 2: High Efficacy (Strong Inhibition & Broad Spectrum)

#### **5. Red Mahogany**

- **Common Name:** Red Mahogany.
- **Place of Origin:** East Africa (studied in Uganda).
- **Source:** Methanol extract of the stem bark.
- **Commercial Production:** Moderate; requires sustainable harvesting of timber trees.
- **Mechanism/Efficacy:** Exhibited the best broad-spectrum activities against both susceptible and resistant strains of *C. albicans*, *C. glabrata*, and *C. tropicalis* compared to other regional medicinal plants. It acts by destroying the fungal cell wall and membrane, leading to the exudation of intracellular substances.
- **Name:** *Khaya anthotheca*

#### **6. Lemongrass**

- **Common Name:** Lemongrass.
- **Place of Origin:** Tropical regions (Asia, Africa, Americas).
- **Source:** Essential oil from the leaves/grass.
- **Commercial Production:** Yes, widely produced.
- **Mechanism/Efficacy:** Highly effective against *C. auris* with MICs as low as 0.02%. It was one of the few oils effective in a **gaseous phase**, meaning its vapors alone could inhibit fungal growth. It generally shows additive effects when combined with antifungal drugs like micafungin.
- **Name:** *Cymbopogon citratus*

#### **7. Mediterranean Cypress**

- **Common Name:** Cypress.

- **Place of Origin:** Mediterranean region.
- **Source:** Essential oil from the leaves.
- **Commercial Production:** Yes, available as an ornamental and oil crop.
- **Mechanism/Efficacy:** Demonstrated the best antibiofilm activity among tested oils in specific studies, with Minimum Biofilm Eradication Concentrations (MBEC) as low as 250 µg/mL against *C. krusei*. It showed fungicidal effects against *C. glabrata* after 12 hours.
- **Name:** *Cupressus sempervirens*

#### 8. Spanish Elm / Inga

- **Common Name:** Inga.
- **Place of Origin:** Brazil (Cerrado region).
- **Source:** Protein extract from the seeds.
- **Commercial Production:** High potential; abundant native tree in Brazil.
- **Mechanism/Efficacy:** Contains a trypsin inhibitor (ILTI) that inhibits the growth of *Candida tropicalis* and *Candida buinensis*. It is notable for showing **no toxicity** in *in vivo* models, suggesting a high safety profile for therapeutic use.
- **Name:** *Inga laurina*

### Tier 3: Moderate to Synergistic Efficacy

#### 9. Hairy Cumin

- **Common Name:** Saharan Cumin, Kemoune essoufi.
- **Place of Origin:** North Africa (Algeria, Morocco).
- **Source:** Essential oil from the fruit.
- **Commercial Production:** Moderate; harvested in arid regions.
- **Mechanism/Efficacy:** Displayed strong inhibitory activity with MIC values as low as 0.162 mg/mL. It contains perillaldehyde and showed a 128-fold reduction in fluconazole MIC when used in combination, aiding in reversing resistance.
- **Name:** *Ammodaucus leucotrichus*

#### 10. Manuka

- **Common Name:** Manuka.
- **Place of Origin:** New Zealand, Australia.
- **Source:** Essential oil from branches and twigs.
- **Commercial Production:** Yes, widely commercialized.

- **Mechanism/Efficacy:** While less effective at killing mature *Candida* compared to Coptis, it displayed a strong inhibitory effect on **germ tube formation** (a key virulence factor) in *C. albicans*, inhibiting filamentation by ~90% at sub-inhibitory concentrations.
- **Name:** *Leptospermum scoparium*

#### 11. Hinokitiol (from Hiba Wood)

- **Common Name:** Hiba, Japanese Cypress.
- **Place of Origin:** Japan.
- **Source:** Monoterpeneoid extracted from the wood.
- **Commercial Production:** Yes, extracted from wood byproducts.
- **Mechanism/Efficacy:** Showed excellent anti-*C. albicans* activity with a MIC of 8.21 µg/mL. It was effective against fluconazole- and caspofungin-resistant clinical isolates and protected *C. elegans* (nematodes) from infection in vivo.
- **Name:** *Thujopsis dolabrata* (Source of Hinokitiol)

## Inclusive Table of Herbs Sorted by Efficacy

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Efficacy Tier	Herb Name (Latin)	Common Name	Origin	Source	Commercial?	Efficacy Highlights
Superior	<i>Cinnamomum verum</i>	Cinnamon Bark	Sri Lanka/Asia	Bark Oil	Yes	Lethal to MDR <i>C. auris</i> at <0.01%; potent fungicidal.
Superior	<i>Thymus leptobotrys</i>	Moroccan Thyme	Morocco	Aerial Parts Oil	Yes	Massive synergy; reduces drug MICs by up to 512-fold.
Superior	<i>Coptis chinensis</i>	Chinese Goldthread	China	Rhizome	Yes	Broad-spectrum fungicidal against 5 <i>Candida</i> species.
Superior	<i>Syzygium aromaticum</i>	Clove	Indonesia	Flower Bud Oil	Yes	Lethal at 0.06%; synergistic with fluconazole.
High	<i>Khaya anthotheca</i>	Red Mahogany	East Africa	Stem Bark	Moderate	Broad spectrum against resistant <i>C. glabrata</i> & <i>C. tropicalis</i> .

High	<i>Cymbopogon citratus</i>	Lemongrass	Tropics	Leaf Oil	Yes	Effective against <i>C. auris</i> ; active in gaseous/vapor phase.
High	<i>Cupressus sempervirens</i>	Mediterranean Cypress	Mediterranean	Leaf Oil	Yes	Strong biofilm eradication; fungicidal against <i>C. glabrata</i> .
High	<i>Inga laurina</i>	Spanish Elm	Brazil	Seed Protein	High Potential	Potent inhibitor of <i>C. tropicalis</i> ; non-toxic in vivo.
Moderate	<i>Ammodaucus leucotrichus</i>	Hairy Cumin	North Africa	Fruit Oil	Moderate	Low MIC (0.162 mg/mL); 128-fold drug synergy.
Moderate	<i>Thujopsis dolabrata</i>	Hiba (Hinokitiol)	Japan	Wood Extract	Yes	MIC 8.21 µg/mL; effective against drug-resistant isolates.
Moderate	<i>Leptospermum scoparium</i>	Manuka	New Zealand	Branch/Twig Oil	Yes	Strong inhibition of germ tube formation (virulence).
Moderate	<i>Mitragyna rubrostipulata</i>	Abria / Nzagu	East Africa	Stem Bark	Moderate	High zone of inhibition; broad-spectrum fungistatic.

Moderate	<i>Origanum compactum</i>	Oregano	Morocco	Aerial Parts Oil	Yes	Synergistic with amphotericin B against <i>C. krusei</i> .
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