

Systematic Review on Effectiveness of Thymus Vulgaris in Candida Albicans

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Abstract:-

➤ *Background:*

Thymus vulgaris has been used to achieve healing, cure chest congestion, and induce saliva since ancient times. The fresh leaves are consumed to relieve sore throats and are traditionally used for numerous skin conditions like oily skin, acne, dermatitis, eczema, and insect bites. It is known to have anti-inflammatory, antimicrobial and antioxidant effects, extensively researched in recent years.

➤ *Aim:*

To determine the effectiveness of Thymus Vulgaris in Candida Albicans.

➤ *Study Design:*

A systematic review of In vitro study using Vulgaris as an effective agent against Candida Albicans. Electronic databases were searched, and 297 articles were obtained, among which four studies were included in this study.

➤ *Result:*

Four studies were included in the systematic review, of which all are in vitro studies. All the studies describe that Thymus Vulgaris has antifungal activity against Candida Albicans.

➤ *Conclusion:*

Thymus Vulgaris has antifungal activity against Candida Albicans and is used for numerous skin conditions like oily skin, acne, dermatitis, eczema, and insect bites.

I. INTRODUCTION

Thymus vulgaris or "thyme" is considered as the most commonly occurring species of the genus "Thymus" (family Lamiaceae), which represents one of the distinguishable plants in many parts of the world, especially throughout the Mediterranean area, North Africa, Asia and Europe.

Since ancient times, thymus Vulgaris has been used to achieve healing, cure chest congestion, and induce saliva; the fresh leaves are consumed to relieve sore throats. The plant is also used as an effective remedy for chest infections (bronchitis, pharyngitis, whooping cough) and to treat worms in children. Thyme oil has been used as a fumigant in places of worship by many ancient civilizations. Thymus vulgaris leaves oil or extract has also been used in the treatment of sore throat, tonsillitis, gum diseases, rheumatism, and arthritis.^{1,2,3}

The Thymus family is well known for its biological compatibility, and it is used in traditional medicine and pharmaceutical preparations. In addition, it is known to have anti-inflammatory, antimicrobial and antioxidant effects, which has been extensively researched in the recent year

Oral thrush -also called oral candidiasis, is a condition in which the fungus Candida albicans accumulates on the lining of the oral cavity. In Morocco, the frequency of candidiasis is quite important, and vulvovaginal candidiasis represents 12.9%..^{4,5} Candida is a normal commensal in the mouth, but sometimes it can overgrow and cause symptoms such as

- White patches on the inner cheeks, tongue, roof of the mouth, and throat.
- Redness or soreness
- Cotton-like feeling in the mouth
- Loss of taste
- Pain while eating or swallowing
- Cracking and redness at the corners of the mouth.

➤ *Risk factors of candida Albicans :*

Candidiasis in the mouth, throat, or oesophagus is uncommon in healthy adults. People who are at higher risk for acquiring candidiasis in the mouth and larynx include children, especially those younger than one month of age, and people with at least one of these predisposing factors:

- Denture wearing patients
- Diabetes patients
- Cancer patients
- HIV/AIDS patients

- Are on antibiotics or corticosteroids regimen, including inhaled corticosteroids for conditions like asthma
- It is taking medications that cause Xerostomia or have medical conditions that manifest as Xerostomia.
- Smokers

Candidiasis in the oesophagus is commonly noticed in immune-compromised patients. This includes patients affected with HIV/AIDS and with conditions like leukaemia and lymphoma. Candidiasis in the oesophagus often manifests along with candidiasis in the mouth and throat. *Thymus vulgaris* essential oil and thymol inhibit biofilms and interact synergistically with antifungal drugs against drug-resistant strains of *Candida albicans* and other candida species. Researchers have been working on determining the effectiveness of *Thymus vulgaris* against *Candida albicans*, and establishing this will pave the way for a cost-effective adjunct for treating oral candidiasis. *Candida albicans* and non-*albicans* *Candida* species are associated with superficial and systemic infections in critically ill patients with weakened immunity. *C. albicans* is very common opportunistic pathogen producing oral, vaginal and or systemic candidiasis.^{6,7}

➤ *Objective:*

To determine the effectiveness of *Thymus Vulgaris* in *Candida albicans*.

II. MATERIALS AND METHODS

➤ *Inclusion criteria*

- Original articles
- In-vitro studies
- Articles on the effectiveness of *Thymus vulgaris* on *Candida albicans*

➤ *Exclusion criteria*

- Articles without open access
- In-vivo studies
- Review articles

➤ *Search Strategy:*

Published clinical trials and original studies on the effectiveness of *Thymus vulgaris* on *Candida albicans* in electronic databases such as Cochrane Central Register of Controlled Trials (CENTRAL), Wiley, Scopus, ScienceDirect, PubMed, MedLine, Gray Literature was collected for review from April 2021 to August 2021.

Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) was used to select the studies. MeSH keywords like “*Thymus vulgaris*, Thyme oil, *Candida*, *Candida Albicans* and dentistry” were used to search collect relevant data. A total of 329 articles appeared with these keywords. After the removal of duplicates, 297 articles were obtained. These articles were screened, and 35 articles were selected to be research-related. Finally, after applying the exclusion criteria, four articles were chosen for review. Figure 1 shows the diagram of several studies identified, screened, assessed for eligibility, excluded and included in the systematic review.

➤ *Search Engines*

- PubMed
- MedLine
- Gray Literature
- Wiley Online Library
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Scopus
- ScienceDirect

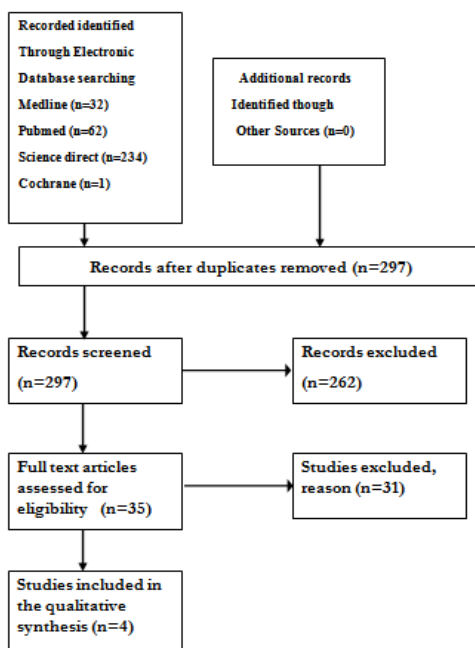


Fig 1:- Flow Diagram showing the numbers of studies identified, screened, assessed for eligibility, excluded and included in the systematic review

S.NO	Author	Year	Inoculation Medium	Duration	Preparations Used	Intervention Used for <i>Candida Albicans</i>
1	H. Jafri I. Ahmed ⁸	2019	Sabouraud dextrose broth/agar (SDB/SDA) and Chrome Candida differential agar	48hrs	Thyme oil extract	Thymol (54.73%) Carvacrol(12.42%) Terpineol (4.00%) Nerolacetate (2.86%) Fenchol (0.5%).
2	Shabeer Shaik Hussain et al. ⁹	2011	dilutions in tubes on liquid Sabouraud	48hrs	Thyme oil extract	Amphotericin B, Minimal inhibitory concentration
3	Mohammadmehdi Fani,Jashd Kohanteb ¹⁰	2017	Sabouraud dextrose agar (SDA)	72hrs	1 mg/mL solution of <i>Thymus vulgaris</i> essential oil	TVO Vancomycin Amikacin Nystatin Nystatin
4	Jonatas Rafael de Oliveira et al. ¹¹	2017	Dulbecco's modified eagle's	24hrs	Thyme glycolic extract	Thyme -50mg/ml Thymol - 10 µg/mL Antimicrobial - 1% DMEMb - Pure

Table 1:- Characteristics of the Interventions in The Included Studies

Table 1: shows the characteristics of the intervention in the included studies. In all the above studies, the effectiveness of *Thymus vulgaris* against *Candida albicans* was evaluated.

S. No	Author And Year	Random Sequence Generation	Allocation Concealment	Selective Reporting	Incomplete Outcome Data	Blinding of Outcome Assessment	Blinding Participants and Personnels
1	H. Jafri I Ahmed,2019 ⁸	-	++	-	?	-	++
2	Shabeer Shaik Hussain et al.,2011 ⁹	-	-	++	-	?	++
3	Mohammadmehdi Fani,Jashid Kohanteb,2017 ¹⁰	-	++	?	-	-	++
4	Jonatas Rafael de Oliveira et al,2017 ¹¹	-	?	-	++	-	++

Table 2:- Bias Analysis of Included Studies

Table 2: shows the bias analysis of all the included studies. It is categorised as high-risk bias "-", low-risk bias "++" and unclear "?". Categorization was done according to the Cochrane risk of bias tools for controlled trials.

Sl. No	Author	Year	Outcome	Result
1	H. Jafri I. Ahmed ⁸	2019	T. Vulgaris constitutes a high percentage of phenolic compounds such as thymol. Thus, it is speculated that the fungicidal and fungistatic activity of T. Vulgaris can be attributed to its main component, the potential to eradicate the sessile cells of C. Albicans. The sessile MICs of antifungal drugs against the test strains exhibited several folds increase in minimum concentration inhibition compared to PMIC.	T. Vulgaris as alternative agents in the treatment of biofilm associated with C. Albicans. Further, their synergistic interaction with antifungal drugs could be exploited against infection caused by the drug-resistant Candida specie ($P < 0.05$)
2	Shabeer Shaik Hussain et al. ⁹	2011	Thymus vulgaris of Moroccan origin showed in vitro and antifungal activity against all tested isolates of C. Albicans. Thymus vulgaris chemotype borneol has an anticandida average effect (CMI 80% between 1 μ L/mL and three μ L/mL)	The Thymus Thymus Vulgaris essential oil has an anticandida activity on C. Albicans strains. The thymus essential oil could be an interesting alternative in anticandida therapies. ($p < 0.05$)
3	Mohammadmehdi Fani, Jashid Kohanteb ¹⁰	2007	Thymus vulgaris oil produced the widest growth inhibition zones (42 + 0.8 mm) and lowest minimum inhibitory concentration (1.9 + 0.2 mg/mL). Thymus vulgaris oil with a mean minimum inhibitory concentration of 16.3 + 4 mg/mL. Minimum inhibitory concentration values of the oil as low as 1.62 + 0 mg/mL ³ to as high as 3300 mg/mL ⁵ for clinical isolates of C Albicans.	The minimum inhibitory concentration of Thymus Thymus Vulgaris oil on C Albicans isolates were 16.3 + 4. The minimum inhibitory concentration of Thymus vulgaris oil on standard strains C Albicans (ATCC 10231) was 16 + 0. ($p \leq 0.05$)
4	Jonatas Rafael de Oliveira et al. ¹¹	2007	In the infection by C. Albicans, no significant reduction of this yeast was observed with the application of thyme oil. The reduction was verified only with nystatin. In this sense, the plant products were not effective in aiding macrophages to control fungal infection. In another study, macrophages RAW 264.7 were pretreated with adequate concentrations of quercetin, a product obtained from plants, and after were infected by C. Albicans.	Thyme oil presented a MIC of 50 mg/mL for C. Albicans. For bacteria, an MIC of 10 μ g/mL for C. Albicans was observed. Regarding infection by C. Albicans, it was noted that the reductions demonstrated by the plant products were not significant in comparison to the control group; nevertheless, nystatin presented the highest percentage of reduction. ($P \leq 0.05$)

Table 3:- Outcome Data as Reported in Included Studies

Table 3: shows the outcome and result of the effectiveness of Thymus vulgaris against Candida albicans in the studies mentioned above. The outcome and results were positive in the above studies showing Thymus vulgaris as a potent adjunct for the treatment of Candida Albicans.

III. DISCUSSION

In this study, 297 articles were obtained. After careful assessment, four clinical trials were selected for further evaluation and discussion.

In the year 2019, H. Jafri, I. Ahmed⁸ conducted an in vitro study on “Thymus vulgaris essential oil and thymol inhibit biofilms and interact synergistically with antifungal drugs against drug-resistant strains of Candida albicans and Candida tropicalis”, which they did with 12 strains and inoculated in Sabouraud dextrose broth/agar (SDB/SDA) and Hirome Candida differential agar for 48hrs and T. Vulgaris as alternative agents in the treatment of biofilm-associated

with C. Albicans. Further, their synergistic interaction with antifungal drugs could be exploited against infection caused by the drug-resistant Candida species.

In the year 2011, Shabeer Shaik Hussain et al.⁹ conducted an in vitro study on Anti candida Activity of the Marketed “Essential Oil of Thymus Vulgaris L and its Concomitant Action with Amphotericin B” in which they did with eight strains and inoculated in dilutions in tubes on liquid Sabouraud for 48hrs and The Thymus vulgaris essential oil has an anticandida activity on C. Albicans strains. Therefore, the thymus essential oil could be an interesting alternative in anticandida therapies.

In 2017, Mohammadmehdi Fani, Jashid Kohanteb¹⁰ conducted an in vitro study on “Antimicrobial Activity of Thymus vulgaris Essential Oil Against Major Oral Pathogens”, which they did with 30 strains inoculated in Sabouraud dextrose agar (SDA) for 72hrs. The minimum inhibitory concentration of Thymus Vulgaris oil on C Albicans isolates were 16.3 + 4. On the other hand, the minimum inhibitory concentration of Thymus Vulgaris oil on standard strains C Albicans was 16 + 0.

In the year 2017, Jonatas Rafael de Oliveira et al.¹¹ conducted an in vitro study on “Thymus vulgaris L. and thymol assist murine macrophages (RAW 264.7) in the control of in vitro infections by Staphylococcus aureus, Pseudomonas aeruginosa, and Candida albicans” in which they did with 24 strains and inoculated in Dulbecco's modified eagle's method for 24hrs and Thyme oil presented MIC of 50 mg/mL for C. Albicans. For bacteria, an MIC of 10 µg/mL for C. Albicans was observed. Regarding infection by C. Albicans, it was noted that the reductions demonstrated by the plant products were not significant in comparison to the control group; nevertheless, nystatin presented the highest percentage of reduction.

IV. CONCLUSION

Thymus Vulgaris has antifungal activity against Candida Albicans and is used for numerous skin conditions like oily skin, acne, dermatitis, eczema, and insect bites.

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