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Biofilm Formation in Oral Candida Albicans Isolates and Evaluation of Myrtus Communis on Cytotoxicity Activity

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Abstract: **Background:** Biofilm formation significantly contributes to the virulence of C. albicans, leading to enhanced resistance against antifungal drugs and persistence during treatment. As antifungal resistance rises, alternative therapies using natural plant extracts are being explored. Plants like Myrtus communis, Mentha spicata, Eucalyptus camaldulensis, and Ceratonia siliqua have shown antifungal potential, making their efficacy and safety assessment crucial for developing new treatments for oral candidiasis. **Method:** During the period between (20/12/2018) to (16/02/2019) fifty oral swabs which diagnosed as oral thrush samples have been collected randomly from pediatric patient who going to Al-Batool Maternity and Children Hospital. Demographic and clinical data were extracted from the medical records using a standardized form. This study aimed to isolate and identify Candida albicans in patients with denture stomatitis, evaluate its capacity for biofilm formation, and investigate the antifungal effect of aqueous Myrtus communis extracts from pomegranate peels, Eucalyptus camaldulensis, Ceratonia siliqua and Mentha spicata. **Results** indicated the highest infection rate (25%) was in infants younger than 1 year. Candida albicans was the organism isolated in 34% of total infections detected. It seemed that feeding practice had affected the prevalence of infections as infants who were exclusively breast fed showed a lower prevalence (13·6%) than those receiving only formula feeds (40·9%).It was also found that 22 isolates were capable of forming biofilms as assessed by interpretation on Gram staining and phenotypic assessment (15–17), which is shown in Figure 4. Of them, 13.6% were classified as strong biofilm producers, 21.3% were moderate, and the others (59.1%) formed low amounts of biofilm. A significant variation occurred in the antifungal activity of tested plant extracts. Ceratonia siliqua had the ability to inhibit Candida albicans only at high concentration (4.5 mm), while pomegranate peels (9 mm), Eucalyptus camaldulensis (9 mm) and Mentha spicata (12 mm) showed moderate inhibition with Myrtus communis being more effective against this microorganism at crude concentrations (23.5 mm). Human lymphocytes were used to assess the cytotoxicity of Myrtus communis extract via MTT assay. Minimum inhibitory concentrations (1000, 500, 250 and 62.5 mg/mL) of the extract prepared in serum-free medium showed that the extract was relatively safe at antifungal concentration. **Conclusion:** prevalence in infants, impact of feeding type, biofilm role in virulence and antifungal resistance; emphasizes Myrtus communis potential as safe antifungal alternative. Condense repetitive content; ensure sequential in-text citations; minor language edits; discuss limitations explicitly.

Key Words: Candida Albicans, Oral Thrush, Medicinal Plants, Biofilm Formation, Aqueous Extracts

INTRODUCTION

The term "Candida," which describes the characteristic white look of lesions caused by this organism, comes from the Latin word candidus, which means "white." Dimorphic fungus, such as Candida species, usually coexist as benign commensals in the human microbiota. However, when the usual microbial balance is disrupted or host defense is weakened, they can transform from yeast cells to invasive hyphal and pseudohyphal forms, becoming pathogenic [1]. Since the onset of HIV infection and the AIDS crisis in the 1980s, research on oral infections caused by Candida albicans has greatly risen [2]. Oral candidiasis, another name for thrush, is believed to be the most prevalent fungal illness worldwide. Every year, an estimated two million

people are affected globally. In addition to oral infections, Candida species can cause infections of the skin, hair, and nails [3]. Oral candidiasis is diagnosed using a variety of mucosal alteration patterns, including erythematous, pseudomembranous, and curd-like plaques or biofilms [4,5]. Although several antifungal drugs have recently been developed to treat fungal infections, their capacity to The ability of the species to live on the mucosal surfaces of healthy individuals has a significant impact on the degree of infection, regardless of the specific species of Candida involved. This persistence is particularly important because bacteria in the oral cavity must withstand the mechanical cleansing impact of a continuous flow of saliva [6]. No single virulence factor has been found to be dominant for Candida, despite the fact that many factors have been linked to accelerating infection. The hydrophobicity of the cell surface and the existence of certain adhesion molecules that promote adherence to oral surfaces are significant contributing factors [7].

Regardless of the kind of Candida involved, the degree of infection is greatly influenced by the species' capacity to survive on the mucosal surfaces of healthy persons. Because microorganisms in the oral cavity must endure the mechanical cleaning action of a constant salivary flow, this persistence is especially crucial [8]. No single virulence factor has been found to be dominant for Candida, despite the fact that several factors have been connected to the infection's development. The hydrophobicity of the cell surface, which encourages adherence to oral surfaces, and the presence of specific adhesion molecules are significant features. [9]. Hydrolysable tannins [HTs], which include most plant polyphenols and account for approximately 92% of their antioxidant activity, are abundant in Punica granatum peel [10]. In addition to producing excellent essential oils [EOs], Mentha species are well known for their diverse biological effects against parasites, bacteria, fungi, viruses, and other pathogens [11,12]. The objectives of this study are to isolate Candida albicans, the causal agent of oral candidiasis and related biofilm, and evaluate the potential antivirulence qualities of extracts from Ceratonia siliqua, Eucalyptus camaldulensis, Myrtus communis, Mentha piperita, and pomegranate peel.

METHODOLOGY

Patient and Specimens' Collection

Fifty samples from children with oral thrush were collected from Baqubah hospitals and labs between December 2018 and February 2019. The pediatric expert chose the patients, who ranged in age from neonates to 12 years old, based on the existence of clinical symptoms. Samples consisting of dextrose agar with chloramphenicol and Sabouraud were injected into the proper culture media. Every plate was cultivated aerobically for 24 to 48 hours at 37°C [13,14]. Diyala University's College of Basic Education and the biology department's microbiological laboratories were recognized and diagnosed.

Limitations subsection explicitly Includes Small sample size; single-center; in vitro plant extract evaluation; limited diversity in children; no longitudinal assessment.

Identification of Candida Isolates

Samples were cultivated on Sabouraud Dextrose Agar and incubated for 24 to 48 hours at 37°C. Gram staining was used to validate the identification of colonies based on their morphology. The germ tube test and CHROMagar Candida were used to further identify Candida albicans; positive findings were revealed by distinctive green colonies.

Directs Examination

On clean slides, oral swab samples were placed, lightly smeared, and then examined under a microscope for developing Candida cells. Additionally, Gram stain was used to stain the isolates to observe how they responded. [15]

Morphological Test

On salted dextrose agar plates, each isolate was cultured for 24-48 hours at 37°C. It is vital to separate the pure Candida colonies to assess their size, shape, colour, and texture.

Germ tube formation

A tiny portion of an isolated colony is inoculated into 0.5 ml of human serum to form a yeast isolate, which is then used to create germ tubes. The suspension was injected at 37°C for three hours. The droplet of this suspension was positioned for examination using light microscopy. A thin lateral hypha thread seems to make up the embryonic tube. Without using any anticoagulants, the serum utilised in this test was created by carefully aspirating it from healthy human blood into sterile test tubes. The samples were properly aspirated from the serum using a sterilised micropipette, placed in a sterilised tube, and maintained in a deep freezer at -8 ºC until needed [16]. The serum was then centrifuged at 300 rpm for 30 minutes.

Determination of Biofilm Formation

The method described in [17] was utilised to evaluate the composition of the biofilm based on the Candidia. 96 sterile well microplates were used to measure the growth of the biofilm. The yeast culture was grafted using a loop into a tube containing 20 ml of brain heart infusion broth medium with glucose (0.25%), and it was then incubated at 37 c for 24 hours. Then, all tubes were diluted by 1:20 using fresh BHIB. 96 sterile polystyrene wells are filled with 200 l of the completed solution. After incubation and rinse, the microscopy at 37ºC for 24 hours was important [18].

Collection of the Plant Materials

A private garden in the city of Baqubah provided the fresh leaves of Myrtus communis, Mentha spicata, Eucalyptus camaldulensis, Ceratonia siliqua fruits, and pomegranate skin. After being transported to the lab, the samples were washed with soft towels to get rid of any dust or insects, dried in the shade for a week while being rotated frequently

to avoid mold growth, weighed, ground up in a mortar and pestle, placed in an airtight bottle, and stored in dissectors for extraction [19].

Prepare the aqueous extract of the plant under study

One liter of distilled water and 25 grams of dried leaves from Myrtus communis, Mentha spicata, Eucalyptus camaldulensis, fruits from Ceratonia siliqua, and pomegranate peel were incubated at 35 degrees in a shaking incubator for 24 hours. After filtering the mixture using filter paper, the extract was dried for 24 hours at 40°C while being spun at 2500 rpm for 10 minutes [20,21].

Evaluation of the Antifungal Activity by the Diffusion Method on Agar

In 2004, CLSI recommended and standardised this method. [22] Muller-Hinton agar, which creates visible zones of inhibition, is the suggested culture medium. Petri dishes containing Muller-Hinton agar are aseptically inoculated using swabs inoculated with Candidia albicanis. Then, using a sterile Pasteur pipette, 6 mm-diameter holes are made. Then, 10 l of each chemical is impregnated into the latter at rates of 25, 50, 75, and 100 mg/ml. After being left at room temperature for 15 minutes, the plates were incubated for 20 to 24 hours at 350 degrees. After incubation, a clear zone develops [23].

Cytotoxic Eeffect of *Myrtus Communis* on Human Lymphocytes

A healthy, nonsmoking donor who did not exhibit any signs of an infectious condition at the time of blood collection provided the lymphocytes. Following dilution with an equivalent volume of phosphate-buffered saline (PBS), the blood was transferred into three milliliters of Ficoll-Paque and centrifuged for twenty minutes at 2,000 g. After being carefully separated from the plasma layer, the lymphocyte layer—also referred to as the white layer or buffy coat—was transferred to a brand-new 15 ml tube. The supernatant was taken from the transferred cells after they had been diluted with 10 millilitres of PBS and centrifuged at 1000 g. 4) and incubated at 37°C for five minutes. The erythrocyte lysis buffer (150 mM NH4Cl, 10 mM NaHCO3, 1 mM EDTA, pH 7) was then used to suspend the cells. PBS was then used to wash the cells three times [24].

The MTT (3-[4,5-Dimethylthiazol-2-yl]-2,5 Diphenyl Tetrazolium Bromide) Protocol

The MTT assay is used to assess the metabolic activity or cellular viability of microcapsules. A water-soluble dye (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) can be converted into an insoluble formazan by metabolically active cells.

Using an MTT ready-to-use kit, the cytotoxic impact of Myrtus communis was assessed:

Kit Contents

MTT solution 1 ml x 10 vials and Solubilization solution 50 ml x 2 bottle.

B- Protocol

- Cells (1x104–1x106 cells/ml) were cultivated in 96 flat-well microtiter plates with a final volume of 200 l of complete culture media (RPMI-1640) per well. The microplate was covered with sterilised parafilm and gently shaken. The plates were incubated with 5% CO2 at 37°C for a whole day
- 2- Following incubation, the media were discarded, and the wells containing PC3 and HdFn cells were supplemented with two-fold serial dilutions of plants (25, 50, 100, 200, and 400 µg/ml). The lymphocyte-containing wells were supplemented with various two-fold serial dilutions of Myrtus communis (1000, 500, 250, 125, and 62.5 µg/ml). on addition to the controls, which were cells grown on serum-free media, triplicates were used for each concentration. The plates were incubated at 37°C with 5% CO2 for the selected exposure duration of 24 hours
- 3- After exposure, ten microliters of the MTT solution were applied to each well. For an additional four hours, the plates were incubated at 37°C with 5% CO2. Each well received 100 µl of the solubilization solution and was left for five minutes after the medium was carefully removed
- 4. An ELISA reader with a wavelength of 575 nm was used to measure absorbance. The viability factor and IC50 (concentration of compound required to cause a 50% reduction in cell viability) were computed for each cell line based on statistical analysis of the optical density data [26]

Determination of Antioxidant Activity by DPPH Assay

An offline 2,2-diphenyl-1-picrylhydrazyl (DPPH) assay was used to assess the antioxidant activity in accordance with Lee's methodology. This test is frequently used to assess a pure chemical compound's capacity to scavenge free radicals. To put it briefly, the control was 200 µL of DPPH reagent added to the first well of a 96-well microplate. For the test samples, 100 µL of plant extracts at various doses (1000, 500, 250, 125, and 62.5 µg/mL) were combined with 100 µL of DPPH reagent. To stop photodegradation, the reaction mixtures were incubated for 30 minutes at room temperature in the absence of light. Following incubation, an ELISA microplate reader was used to measure the absorbance at 514 nm. 100% methanol served as the blank control. The following formula was utilized to determine the percentage of DPPH radical scavenging activity: [26].

$$\% \text{ Scavenging Activity} = A_{control} (A_{control} - A_{sample}) \times 100$$

Statistical Analysis

Data analysis and visualization were conducted using GraphPad Prism, version 9, presenting results as mean±SD. A Student's t-test was utilized to compare means of two independent groups, suitable for data that are approximately normally distributed with similar variances. For multiple

group comparisons, a one-way ANOVA was applied to assess significant differences among means. If ANOVA showed a significant effect, post hoc tests like Tukey's test were employed to pinpoint specific group differences while controlling for type I error, with statistical significance defined as a p-value <0.05.

RESULTS AND DISCUSSION

Distribution of Children with Oral Thrush by Age and Sex

Patients with oral candidiasis ranged in age from less than one year to 12 years, with a male-to-female ratio of 1.27:0.78 (Figure 1). The highest colonization was observed in children under one year, with males and females accounting for 53.6% and 45.5% of cases, respectively. The lowest proportion was found in males aged 5–12 years, at 7.1%, while females in the 1–5-year age group showed the lowest percentage at 13.6%. These results are consistent with previous studies [27,28], which reported that younger children are more frequently affected by oral *Candida* infections than older children. However, some findings differ from other published research, indicating variability in infection patterns across populations.

Distribution of Candidia albicanis according to the Type of Feeding

Figure 2 displays the distribution of Candidia albicanis isolates based on feeding type. It revealed that children who rely on breastfeeding had the lowest prevalence of the fungus (14%), while children who rely on artificial or mixed feeding had the lowest prevalence (30,31%) [29,30].

The lowest prevalence of oral *Candida* colonisation was observed among exclusively breastfed infants, particularly those who did not use pacifiers or rubber nipples. In contrast, feeding bottles and pacifiers were identified as significant contributing factors among artificially fed infants. The frequent use of bottle nipples— especially when exposed to hot liquids and maintained under poor hygienic conditions— may irritate the oral mucosa and increase susceptibility to

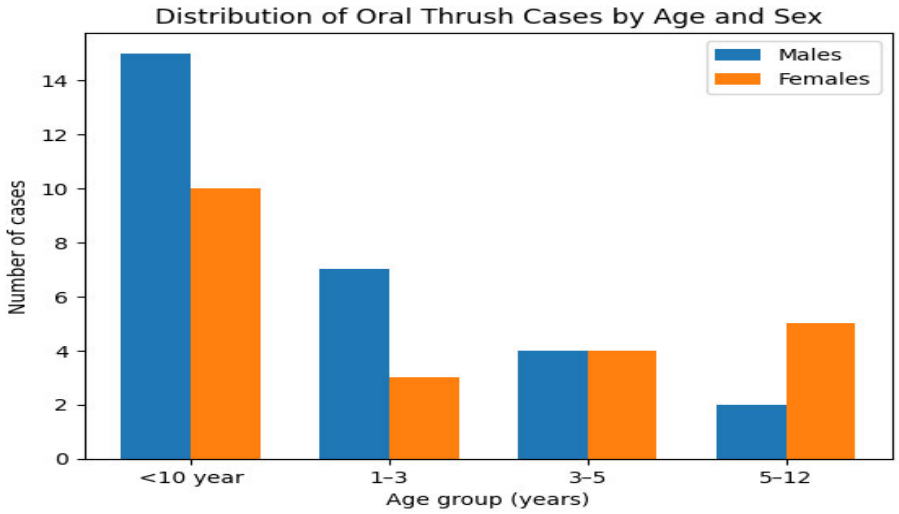

Figure 1: Distribution of Oral Thrush Cases by Age and Sex

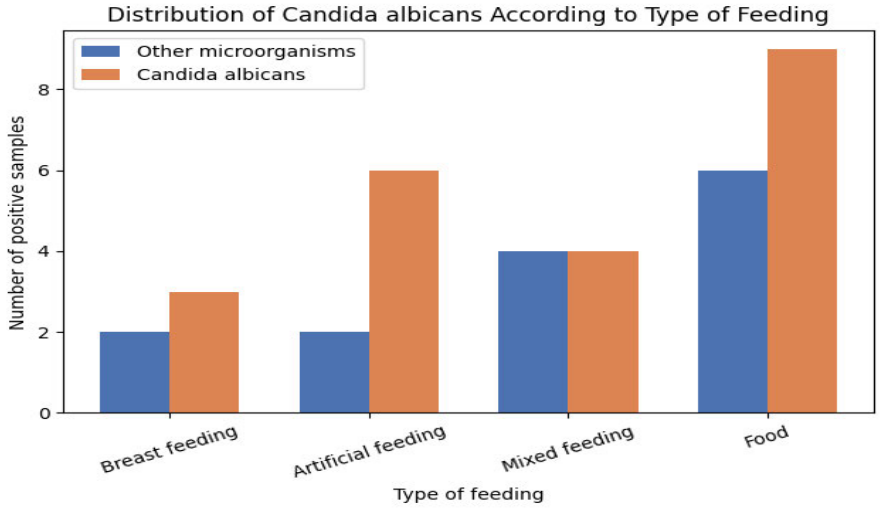

Figure 2: Distribution of Candidia Albicanis according to the Type of Feeding

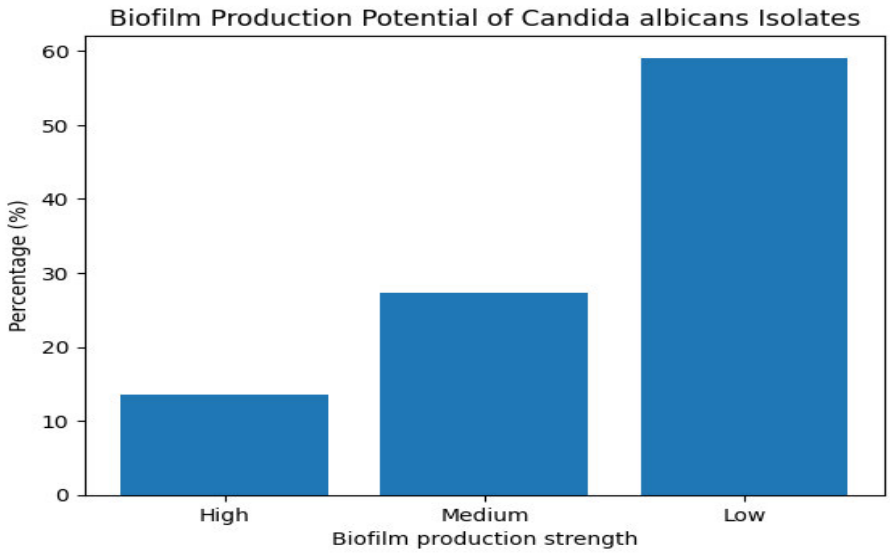

Figure 3: Shows the Number and Percentage of Candidia Isolates according to their Biofilm Production Strength

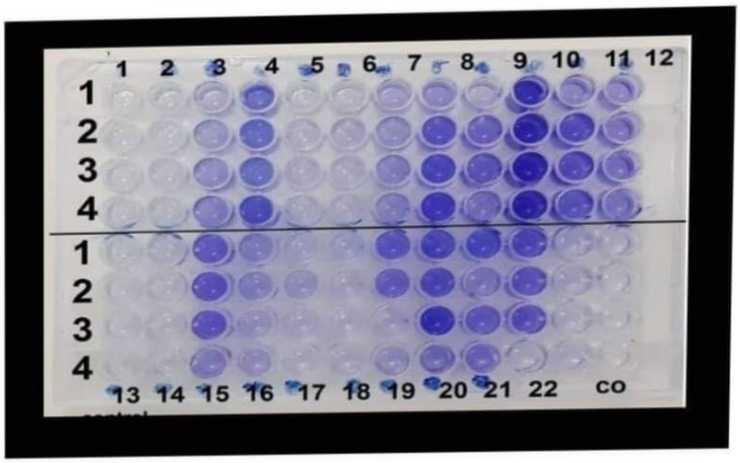

Figure 4: Biofilm Strength Compared to the Control

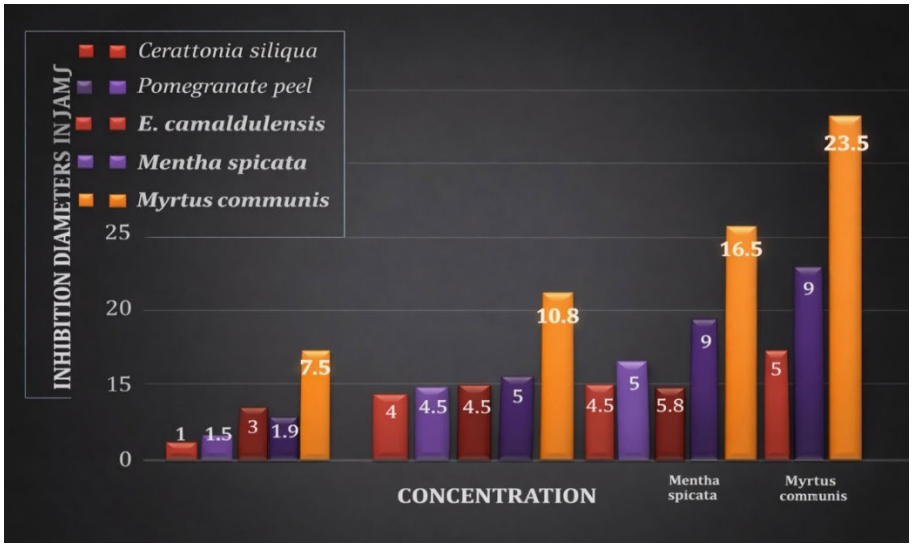

Figure 5: Effect of Aqueous Plant Extracts at Different Concentrations on *Candida Albicans* Isolates

infection [31]. Breast milk contains protective components such as lysozyme and lactoferrin, which provide natural antimicrobial activity and help prevent the colonisation of *Candida* species in the oral cavity of breastfed infants [32].

Biofilm Produced by Candida Isolates

The ability to form biofilm was detected in all 22 positive *Candida* spp. isolates obtained from oral thrush cases, as illustrated in Figure. 3 and Figure. 1. Among the 22 *Candida albicans* isolates, 3 (13.6%) were classified as strong biofilm producers, 6 (27.3%) as moderate producers, and 13 (59.1%) as weak producers. In total, 32 out of 39 (51.3%) *C. albicans* isolates demonstrated biofilm-forming capacity. Similarly, 21 out of 36 (58.3%) non-*albicans Candida* isolates were capable of forming biofilm. Overall, while variations were observed in the strength of biofilm production among isolates, the findings consistently demonstrate that biofilm formation is a common virulence attribute among both *C. albicans* and non-*albicans Candida* species Figure 4.

Cell wall proteins such as ALS1, ALS3, and HWP1 play a critical role in adhesion during the initial stage of *Candida* biofilm formation, which involves attachment to host tissues or medical device surfaces [33]. These adhesins facilitate stable colonization and biofilm maturation. In addition to colonising implanted medical devices and compromising their function, biofilm formation significantly increases antifungal resistance and contributes to evasion of host immune defenses. Consequently, biofilm-associated infections are often persistent and difficult to eradicate [34].

Effect of Plant Extract on Candidia Albicanis

The present study aimed to identify potential plant-based alternatives to conventional antifungal drugs used in the treatment of fungal infections. The results demonstrated a noticeable inhibitory effect of aqueous plant extracts against *Candida albicans*. The inhibition zone diameters (mm) at concentrations of 25%, 50%, 75%, and 100% were as follows:

- *Myrtus communis*: 7.5, 10.8, 16.5, and 23.5 mm
- *Mentha spicata*: 1.9, 5, 5.8, and 12 mm
- *Eucalyptus camaldulensis*: 3, 3.5, 4.5, and 9 mm
- Pomegranate peel extract: 1.5, 4.5, 6, and 9 mm
- *Ceratonia siliqua*: 1, 4, 4.5, and 5 mm

As shown in Figure 5, the inhibitory activity increased with increasing extract concentration. Among the tested plants, *Myrtus communis* exhibited the highest inhibition rate, whereas *Ceratonia siliqua* showed the lowest antifungal activity against *C. albicans*.

Figure 5 illustrates the antifungal activity of aqueous extracts of *Myrtus communis*, *Mentha spicata*, *Eucalyptus camaldulensis*, pomegranate peel (*Punica granatum*), and *Ceratonia siliqua* at concentrations of 25%, 50%, 75%, and 100% against *Candida albicans* isolates [35]. The findings show that inhibition increases with concentration, with 100% exhibiting the highest activity. The essential oil composition of Myrtus communis may be responsible for its potent antifungal action. While other types (like Italian myrtle oil) are mostly made up of α-pinene and 1,8-cineole, myrtle oil is rich in bioactive components like linalool and linalyl acetate. The variations in antimicrobial activity seen among myrtle oils could be explained by variations in the percentage composition of these components [17].

The antimicrobial qualities of secondary metabolites obtained from medicinal plants have drawn more attention in recent years. Traditional herbal medicine has long been used worldwide for the treatment of various infectious diseases, and plant-derived antimicrobial agents continue to offer promising alternatives to conventional therapies. The antifungal activity of pomegranate peel has also been widely reported. It has been shown that pomegranate peel extract at a concentration of 20 mg/mL completely inhibited fungal spore germination and reduced mycelial growth by 75.5% [35]. The antioxidant and antimicrobial activities of pomegranate peel are mainly attributed to its high content of phenolic acids, flavonoids, and tannins—particularly ellagitannins, which are considered the primary contributors to its bioactivity. Additionally, both in vitro and in vivo studies have demonstrated the effectiveness of aqueous pomegranate peel extract against brown rot disease caused by *Monilinia laxa* and *Monilinia fructigena*. Gram-positive and Gram-negative bacteria and fungi were reported to be significantly controlled by pomegranate peel water extract [14]. The presence of tannine in Ceratonia siliqua was likely the active ingredient to adsorb toxins and precipitate proteins, according to our data, which revealed that boiling water extract of Ceratonia siliqua reduced the development of Candida in the agar diffusion assay and prevented the colonisation of Candida. The most frequently removed components of Ceratonine siliqua upon hydrolysis are arabinose, galactose, glucose, mannose, xylose, and different uronic acids [36]

Cytotoxic Effect of *Myrtus Communis* on Human Lymphocytes

The cytotoxic effect of *Myrtus communis* extract on human lymphocytes was evaluated using the MTT assay after 24 hours of exposure. The results demonstrated that the biologically synthesised *Myrtus communis* extract did not significantly reduce lymphocyte viability at the tested concentrations (125, 250, 500, and 1000 µg/mL) compared to the untreated control group. [37].

There was no discernible dose-dependent decline in cell viability using the MTT test, a popular technique for evaluating in vitro cytotoxicity in cell culture investigations. Although cellular viability somewhat decreased at higher concentrations, the changes were not statistically significant, indicating limited cytotoxic potential. These findings suggest that the naturally occurring extract of Myrtus communis is rather safe for healthy human lymphocytes in the conditions studied. [38] Because of this, it could be a good and safe alternative for applications that don't require a lot of cytotoxicity to healthy cells. Figure 6 shows the effect

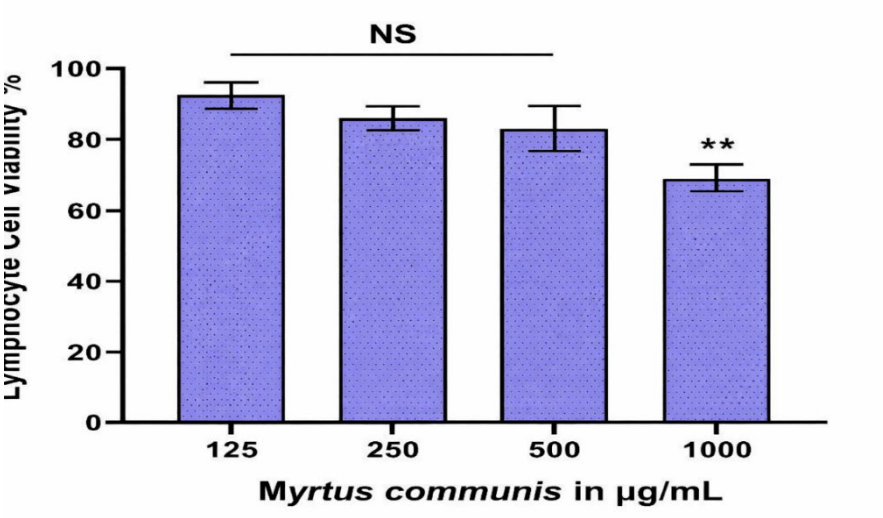

Figure 6: Myrtus Communis-Mediated Impact on the Viability of Human Lymphocytes. Following Treatment with Varying Concentrations (125, 250, 500, And 1000 µg/Ml), The Mtt in Vitro Test was used to Calculate Cell Viability (%). the Mean ± Sd is used to Express the Data (N = 3). At 125–500 µg/Ml, Statistical Analysis Revealed Non-Significant Differences (Ns), but at 1000 µg/Ml, Viability Significantly Decreased (**p<0.01).

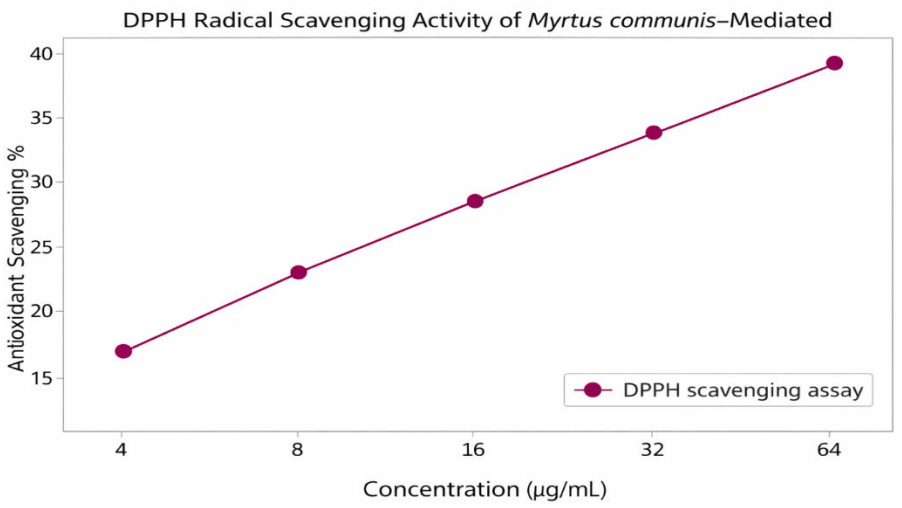

Figure 7: Effect of *Myrtus communis*–mediated) Determination of Antioxidant Activity by DPPH Assay

of Myrtus communis therapy on lymphocyte viability as assessed by the MTT assay following a 24-hour incubation period. According to the MTT assay, the most current study showed that Myrtus communis extract at doses ranging from 125 to 1000 µg/mL did not significantly lower the viability of human cells after 24 hours of exposure. [39]. The absence of a noticeable dose-dependent cytotoxic effect suggests that the extract has a satisfactory safety record with functional human immune cells in the circumstances under investigation. The MTT test, which measures mitochondrial metabolic activity, is well recognised as a reliable and sensitive method of evaluating in vitro cytotoxicity. Unaltered metabolic activity indicates that cellular integrity and function have been maintained, as live cells use mitochondrial dehydrogenase enzymes to convert MTT into formazan crystals. [40]. The low cytotoxic potential of Myrtus communis was supported by the current study's conclusion that a slight reduction in cell viability at greater amounts was not statistically significant. These results are in line with earlier research showing that Myrtus communis has antibacterial, antioxidant, and anti-inflammatory qualities while being largely beneficial to healthy mammalian cells. Myrtus communis's abundant supply of phenolic compounds, flavonoids, tannins, and essential oils is partially to blame for its biological activity and medicinal potential. Numerous studies have demonstrated that polyphenolic chemicals originating from plants can have very little cytotoxicity against human cells in good health, while yet showing selective antibiotic actions [41].

Determination of Antioxidant Activity by DPPH Assay

The DPPH radical scavenging assay used in this study shows that Myrtus communis-mediated nanoparticles have strong concentration-dependent antioxidant activity. The findings

demonstrated a progressive rise in scavenging activity from the lowest concentration (4 µg/mL) to the greatest concentration (64 µg/mL), suggesting that the concentration of plants improved free radical neutralization. [42]. The DPPH assay is frequently used to assess a bioactive chemical or nanomaterial's ability to donate hydrogen or transfer electrons. A decrease in DPPH absorbance indicates the examined material's ability to scavenge free radicals. Because of the M. communis phytochemical components utilized in the synthesis process, the observed increase in the scavenging % suggests that the generated plants have effective electron-donating capabilities. Figure 7. To evaluate a bioactive compound's capacity to transfer electrons or donate hydrogen, the DPPH test is commonly used. A decrease in DPPH absorbance indicates the examined material's ability to scavenge free radicals. [43]. The M. communis phytochemical substances used in the green synthesis approach are probably responsible for the observed increase in the scavenging %, which shows that the generated nanoparticles have superior electron-donating properties. Myrtus communis, which is abundant in flavonoids, tannins, and phenolic compounds, is known to possess potent antioxidant properties [44]. During the production of nanoparticles, these phytochemicals may act as capping and reducing agents, enhancing the particles' stability and surface reactivity. This synergistic effect may be responsible for the slow increase in radical scavenging activity seen in this study.

CONCLUSIONS

The current study underscores the significance of Candida albicans in causing oral thrush in kids, especially those less than a year. Given that formula-fed children had higher infection rates than exclusively breastfed newborns, findings showed that feeding type is a major risk factor. It was determined that the isolates' varied capacities to produce biofilms made biofilm formation a common virulence factor. The existence of biofilm highlights the therapeutic significance of addressing infections linked to biofilms since it increases resistance to antifungals and enhances persistence inside the host. Myrtus communis showed the highest inhibitory impact in a concentration-dependent manner, although all of the aqueous plant extracts evaluated in this study indicated detectable antifungal activity against Candida albicans. Various levels of antifungal activity were also demonstrated by other extracts, such as Ceratonia siliqua, Eucalyptus camaldulensis, Mentha spicata, and pomegranate peel (Punica granatum).

Importantly, Myrtus communis extract showed no toxic effects on normal human lymphocytes at antifungal doses, indicating acceptable biocompatibility under the investigated conditions, depending to the cytotoxicity evaluation using the MTT assay.

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