

Abstract

The transition of *Candida albicans* from yeast to hyphal form is a critical determinant of its pathogenicity, enabling the fungus to invade host tissues and form biofilms resistant to antifungal treatments. Honey has welldocumented antifungal properties, yet its effect on C.

albicans morphogenesis remains underexplored. This study aims to investigate whether honey can inhibit or reduce the yeast-to-hyphal transition of *C. albicans*, potentially offering a novel adjunct to antifungal therapies. The experiment will use *C. albicans* strain SC5314, treated with varying concentrations (10%, 25%, and 50%) of high, low, and medium bioactivity honey, with a control group of untreated cells. After incubation at 37°C for 2–4 hours, morphological changes will be assessed using microscopy, and the percentage of yeast versus hyphal forms quantified. The findings could reveal whether honey inhibits the morphological transition, providing insights into its potential role in managing C. *albicans* infections and reducing its virulence. This research addresses a significant gap in the literature and may contribute to the development of natural treatments for fungal infections

Introduction

Candida albicans is a fungus that normally lives harmlessly on human mucous membranes, like the GI tract, mouth, and vagina. But when immunity weakens, C. albicans shifts from a harmless yeast to an invasive hyphal form, which drives its virulence (Nett et al., 2011). The hyphal form invades tissues and resists immune attacks, making it key to pathogenicity and biofilm formation (Gow et al., 2011; Kadosh & Johnson, 2005).

C. albicans infections can be mild or life-threatening, especially in immunocompromised people like those with HIV/AIDS, cancer, or organ transplants (Pappas et al., 2018). Biofilms on medical devices make treatment harder since they're highly resistant to antifungals (Finkel & Mitchell, 2011). Triggers like temperature, pH, and nutrients push C. albicans to switch forms, regulated by pathways like MAP kinase and cAMP/PKA (Kadosh & Johnson, 2005; Finkel & Mitchell, 2011).

Manuka honey is known for strong antimicrobial effects, including antifungal action against *Candida* species (Berdy, 2005; Al-Waili et al., 2012). While honey's ability to fight fungal growth is well-documented, its role in preventing the yeast-to-hyphal switch in *C. albicans* is not well understood. Exploring this could offer new strategies for treatment, especially as antifungal resistance grows (Al-Waili et al., 2012).

Honey's antifungal power comes from its sugars, low pH, and bioactive compounds like hydrogen peroxide, phenolic acids, and methylglyoxal (Berdy, 2005). These work together to damage fungal cells and block growth. Studies show honey stops *Candida* growth and biofilm formation, both vital to its resistance (Al-Waili et al., 2012; Salom et al., 2015). Honey's antioxidant and anti-inflammatory effects may also boost its therapeutic value (Al-Waili et al., 2012).

Even with this evidence, little is known about honey's effect on C. albicans' morphological switch. While it blocks growth and biofilms, its impact on the yeast-to-hyphal transition is underexplored. This study aims to fill that gap and assess honey's potential to control C. albicans virulence.



Impact of Honey on the Morphological Transition of Candida Albicans

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Objective

The goal of this study is to determine whether honey can prevent or reduce the yeast-tohyphal transition in *Candida albicans*, potentially limiting its virulence and offering a natural alternative to antifungal treatments.

Materials and Methods

Step	Description
Sample Prep	SC5314 cultured in RPMI
Honey Addition	Honey types & concentrations prepared (local Texas honey and 10%,25% and 50% concentrations)
Incubation	37°C for 2–4 hrs
Microscopy	Morphology assessment through counting

Figure 1. General overview of materials and quick methods

• pH Conditions:

• pH 7.2: RPMI + HCl

• pH 8.6: RPMI alone

Preparation of Different pH Conditions



• pH 13.4: RPMI + NaOH **RPMI + HCI (pH 7.2)** • Honey Concentrations: Add HCI dropwise to RPMI • 10%, 25%, 50% until pH reaches 7.2. • Low, Medium, High bioactivity honey **24-Well Plate Layout:** RPMI Alone (pH 8.6) • Assign wells for each pH + honey Use RPMI without concentration adjustments. • Include controls: RPMI only, RPMI + Fluconazole RPMI + NaOH (pH 13.4)

Add NaOH dropwise to RPMI until pH reaches 13.4.

• **Inoculation:** *Candida albicans* SC5314 added to each well

• **RPMI Medium** prepared for all groups.

- **Incubation:** 37°C for 2–4 hours
- Microscopy: Check for yeast and hyphal forms

Figure 2. Preparation of RPMI for Candida Albicans growth Medium



Results





Figure 3. Observation of Candida Albicans after 2 & 4 hours incubation time with different pH



Figure 4. Observation of Candida Albicans after 4 hours of incubation with Local Texas honey samples.



Figure 5. Observation of Candida Albicans in control conditions with different pH after 4 hours.

Condition	%	Ye

Condition	% Yeast	% Hyphal
RPMI + HCl	High Yeast	Low Hyphal
RPMI Alone	Moderate Yeast	Moderate Hyphal
RPMI + NaOH	Low Yeast	High Hyphal

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Results

Growth of Candida Albicans Hyphal form in 2 hours and 4 hours with Honey Intervention



Figure 6. Initial observation of Candida Albicans in Hyphal form observed and counted after 2 hours and 4 hours.

Discussions

- The data indicate that honey can inhibit or significantly delay the morphological transition of *Candida albicans* from yeast to hyphal form.
- Environmental factors, including pH and temperature, influenced hyphal development, with lower pH and cooler temperatures slowing the morphological progression.
- Variability between honey types suggests that both bioactive compound composition and pH may contribute to honey's antifungal activity.
- A limitation of this study was distinguishing between true inhibition of morphogenesis and reduced cell viability, highlighting the need for viability staining in future experiments.
- Future directions include gene expression analysis, testing honey in combination with fluconazole, and conducting zone of inhibition assays to clarify honey's antifungal mechanisms.
- These findings support the potential of honey as a natural antifungal agent, capable of maintaining *Candida albicans* in its less pathogenic yeast form.

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