Drug Repurposing in Mycology: Finasteride and NSAIDs Efficacy as Potential Antifungals Against Yeast Strains Isolated From the International Space Station

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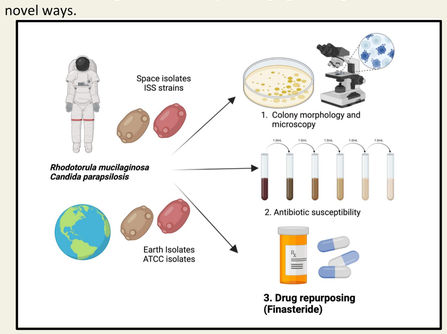
1. Abstract

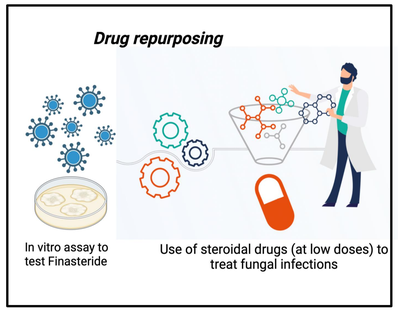
The rise of antimicrobial resistance has exacerbated the threat of fungal infections, especially among immunocompromised individuals. Yeasts, typically harmless commensals, can turn into formidable pathogens under stress conditions similar to those found in space, such as variable temperatures, altered oxygen levels, and microgravity. This scenario is particularly concerning for astronauts, making otherwise non-threatening yeast strains into significant health risks. Traditional antifungals, including azoles and polyenes, often fail to combat these infections effectively, highlighting the urgent need for alternative therapeutic strategies. Repurposing non-steroidal anti-inflammatory drugs (NSAIDs) emerges as a swift, cost-effective, and safe approach to address this challenge. This study explores the antifungal potential of Finasteride, Flufenamic acid, and Tolfenamic acid against four yeast strains isolated from the International Space Station: *Candida parapsilosis, Candida albicans, Cryptosporidium laurentii,* and *Rhodotorula mucilaginosa.* Our goal is to identify effective treatments for potential fungal infections by leveraging existing medications in novel ways.



Strain Name	Type Strain/Identifier	Source/Sample type
Candida parapsilosis *Candida albicans* *Cryptococcus laurentii* *Rhodotorula mucilaginosa*	Earth isolate	American Type Collection (ATCC) Case of Sprue
Candida parapsilosis *Candida albicans* *Cryptococcus laurentii* *Rhodotorula mucilaginosa*	Space Isolate	Expeditions ISS 501820 ISS 140720006-1

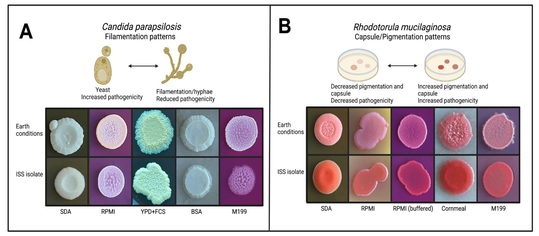
Strains selected for this study

2. Introduction and Methods



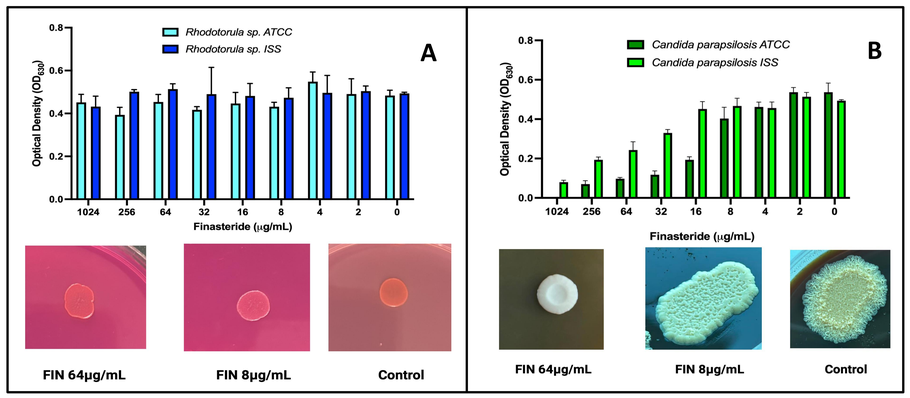
Drug repurposing, is the process of identifying new uses for existing drugs that are already approved for other indications. Instead of developing entirely new drugs from scratch, researchers explore the potential of existing drugs to treat different diseases or conditions.
There are several reasons why drug repurposing is important:

1.Cost and Time Efficiency
2.Reduced Risk
3.Addressing Unmet Medical Needs
4.Expanding Treatment Options
5.Leveraging Existing Knowledge
6.Sustainability



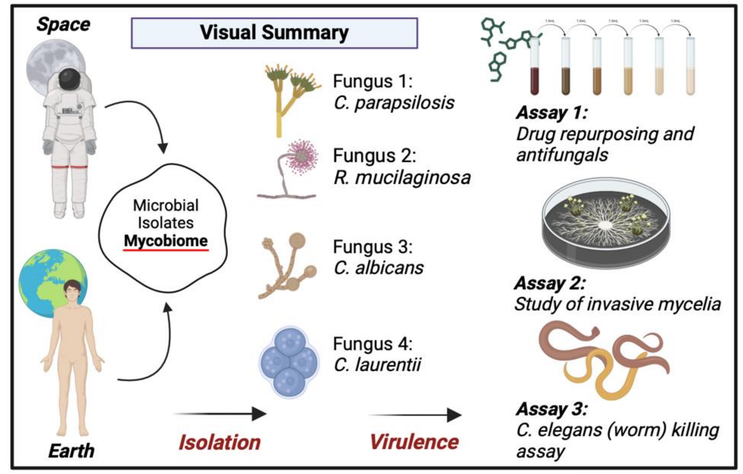
- Previous results have shown that fungal strains are very resistant to traditional antifungals (*Fluconazole, Amphotericin B and Caspofungin*)
- Resistant to antifungals is linked to fungal phenotype switch, including formation of smooth vs wrinkly colonies

Preliminary Results



Antimycotic susceptibility tests. Finasteride was effective against *Candida* growth but not *Rhodotorula*. The isolates from the ISS demonstrated a higher resistance to Finasteride.

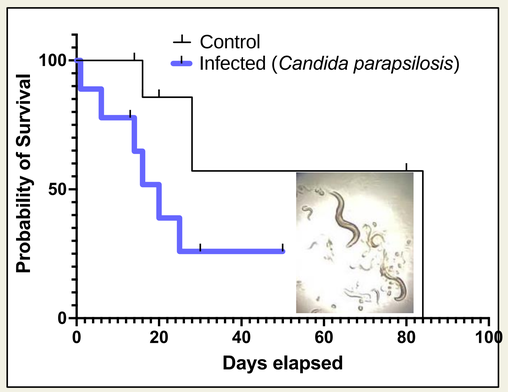
Methodology

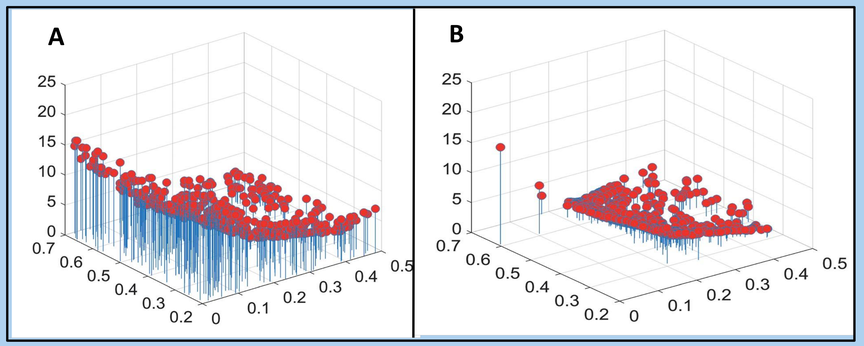


- Drug repurposing assays → Testing Flufenamic acid, Tolfenamic acid, Finasteride, Simvastatin, Ketorolac, Chloramphenicol, Gram positive antibacterials.
- MIC and MFC (Minimum Inhibitory and Minimum Fungicidal Concentrations are determined.
- Observation of Filamentation and Colony morphology
- Virulence infection assays using a Nematode killing assay (using *C. elegans* as a model study).

3. Results

Virulence Infection assays using the model system *C. elegans*.
100 worms were grown for 7 days and 5 fields (approx.. 30 worms were selected an infected with a control strain). After 20 days viability was calculated and observed against a non-infected control.

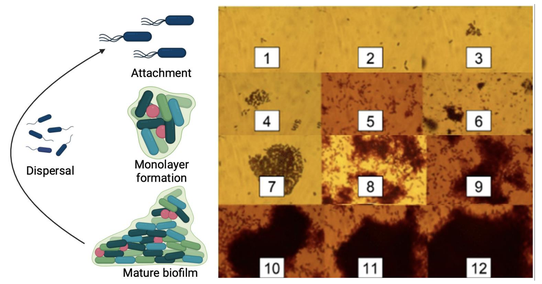




Antimycotic susceptibility tests. Flufenamic acid (A) and Tolfenamic acid (B) two NSAIDs (Non-Steroideal Antiinflammatory Drugs) were tested for their efficacy against *C. parapsilosis* **A** ISS and **B** earth or ATCC strains. More resistance is observed in ISS isolate.

4. Conclusion and Future Perspectives

- Analysis of resistance in microbial communities or Biofilms
- Gene expression analysis of resistant strains
- Combinational (synergistic) analysis of two of more drugs.



Acknowledgements

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