Synthesis of Triazole-Heterocycle Fenarimol Analogues for the Use of Treatment of Eumycetoma

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Introduction

Mycetoma is a rare disease that includes chronic infection of the skin and subcutaneous tissue. It has been given the ‘neglected tropical disease’ designation by the WHO due to it being mainly prevalent in poor populations in remote areas. Today, the WHO designates 20 of these diseases that affect approximately 1.5 billion people a year. Mycetoma infections caused by bacteria are called actinomycetoma, while fungal infections are called eumycetoma. These infections have poor treatment options that are generally only 25–35% effective and are largely unaffordable/unobtainable to the poor populations that need them. With this project, we proposed and planned the synthesis of potential treatments. Due to the pandemic, we were unable to physically synthesize/test these compounds.

Eumycetoma

Prevalence of Mycetoma

![Map showing the prevalence of mycetoma](https://onlinelibrary.wiley.com/doi/fig/10.1111/ced.13642)

- **No data**: <0.01–100,000
- **0.01–0.10,000,000**: 0.01–10,000,000
- **0.10,000–1,000,000**: 0.10,000–1,000,000
- **≥1,000,000**: ≥1,000,000

![Image of eumycetoma infected skin with an arrow pointing to the infectious fungal grain](https://onlinelibrary.wiley.com/doi/fig/10.1111/ced.13642)

- Infection occurs from introduction of fungus to an open wound – *Madurella mycetomatis*
- Symptoms include:
  - Swelling of tissue
  - Sinus discharge
  - Colony formation of infectious agent called grains
- Removal of infected tissue via surgery/amputation is most common treatment, leads to inability to work and stigma
- Modern treatments are either too expensive or not effective and are potentially dangerous

Methodology

**Treatment Goals**
- Develop a novel antifungal that is both safe and effective
- Cheap to make and obtain
- Specific to Eumycetoma

**Promising Research as a Baseline**
- We looked at several studies involving effective antifungal/mycetoma effects to help us create target treatment compounds

![Figure 3. Fenarimol (top) analogues were discovered by Lim et al to be potent against M. mycetomatis. Heterocyclic triazoles (bottom) were effective vs. fungal agent Candida albicans, the most common infectious fungal agent. Considering the fenarimol’s specificity to the main fungal agent of eumycetoma and the triazoles noted antifungal properties, we looked at synthesizing fenarimol analogues containing triazole](https://onlinelibrary.wiley.com/doi/fig/10.1111/ced.13642)

**Proposed Molecules**

![Figure 4. The top three molecules were proposed with only cost effectiveness in mind. The bottom two compounds were designed with the knowledge that the presence of chlorine produced more effective treatments but were also much more expensive.](https://onlinelibrary.wiley.com/doi/fig/10.1111/ced.13642)

**References**

5. Madurella graminea; *M. mycetomatis*

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Questions?

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