**Objectives**:

The emergence of dermatophytosis caused by *Trichophyton indotineae* (formerly *Trichophyton mentagrophytes genotype* VIII)  is a growing global concern given the propensity of this pathogen to cause severe and recalcitrant disease, often occuring in case clusters, and the fact that *T. indotineae* is frequently terbinafine-resistant. *T. indotineae* re-emerged in Australia in 2023 and has subsequently been isolated by numerous diagnostic laboratories across the country. Since antifungal susceptibility testing is not routinely performed for dermatophytes and data on the susceptibility profile of T. indotineae remain limited, this study aimed to determine the *in vitro* activity of five antifungal agents including new agent,olorofim, against clinical isolates of *T. indotineae*.

**Materials & Methods:**

Thirty-six clinical isolates of *T. indotineae* from the culture collection of a single diagnostic mycology laboratory in Sydney Australia were studied. All isolates were confirmed as *T. indotineae* by DNA sequencing of the internal transribed spacer region. Antifungal susceptibility testing (AFST) was performed according to Clinical and Laboratory Standards Institute reference standard (CLSI M38-A3) using specified quality control (QC) and reference strains. Drugs tested included itraconazole, voriconazole, posaconazole,terbinafine and olorofim at concentrations of 0.008-4 mg/L. All plates were incubated at 30oC for 96 hours and the MIC endpoint was read visually as 80% inhibition of growth compared to the control for itraconazole, posaconazole, voriconazole and terbinafine, and 100% inhibition for olorofim.

**Results**:

MIC values for all QC and reference strains were within the published range for each antifungal agent. Of 36 *T. indotineae* strains 24 (66.7%) had MICs ≥2 mg/L to terbinafine (GM: 0.7 mg/L ; MIC ranges: 0.015-4 mg/L). By comparison, MICs to itraconazole, posaconazole and voriconazole were low as follows: GM 0.06 mg/L for itraconazole and posaconazole, and GM 0.019 mg/L for voriconazole. Table 1 summarises the MIC ranges and GM MIC values for all isolates studied. Olorofim displayed the greatest *in vitro* activity (MIC range: 0.03-0.015 mg/L; GM: 0.01 mg/L).

**Conclusions**:

Management of dermatophytosis is becoming increasingly challenging following the global emergence of terbinafine resistant *T. indotineae*. This is the first study to report susceptibility data for *T. indotineae* isolates from Australia. High MICs value of Terbifain among *T. indotinea* are consistent with global report, where 70% of strains show resistance. These findings highlighted the importance of performing antifungal susceptibility testing in clinical setting against this emerging pathogen to control and efficient mangement of infection. Whilst olorofim was the most potent antifungal tested (GM: 0.01 mg/L; MIC90: 0.03 mg/L) the azoles also demonstrated good activity particularly both itraconazole and posaconazole exhibited the low GM MIC of 0.06 mg/L. Inferring that they may be satisfactory alternatives where terbinafine MICs are high. Further the new antifungal olorofim has shown significant potential activity against *T. indotineae*.

Table 1. In vitro anti -fungal activity of drugs against clinical *T. indotineae* strains

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| --- | --- |
| Species(N) |  Drug name MIC range (mg/L) GM MIC (mg/L) MIC50 MIC90 |
| *T. indotineae*(36) | Itraconazole 0.007-0.5 0.06 0.09 0.5 Olorofim 0.03-0.015 0.01 0.015 0.03Posaconazole 0.007-0.5 0.06 0.06 0.25Terbinafine 0.015-4 0.7 4 4Voriconazole0.03-2 0. 19 0.25 0.5 |