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# *Candida auris* is highly *in vitro* susceptible to APX001A in EUCAST antifungal susceptibility testing


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## Objectives

*Candida auris* is a multidrug-resistant yeast that is rapidly emerging as a significant cause of nosocomial infections. Here, we report the susceptibility of *C. auris* to APX001A, the active moiety of the investigational antifungal drug APX001. APX001A inhibits the conserved fungal inositol acyltransferase enzyme Gwt1, thereby preventing GPI-anchored protein maturation and compromising fungal growth.

## Materials/methods

**Laboratory methods:**

1. Isolates: 122 Indian clinical *C. auris* isolates and the *C. auris* control strains KCTC17809, KCTC17810 and JCM15448
2. EUCAST E.Def 7.3.1 using Cell-culture treated Nunc plates (ThermoFisher cat. no. 167008)
3. Plates preparation:
   - ISO method for APX001A and fluconazole
   - Serial two-fold dilution for amphotericin B, anidulafungin, micafungin, isavu-, itra-, posa and voriconazole;
   - Stored at –80 °C for ≥24 h prior to use
4. Antimycotics and concentrations: APX001A; 0.5-0.0005 mg/L, anidulafungin and micafungin; 32-0.002 mg/L, amphotericin B, vori-, isavu- and itraconazole; 8-0.008 mg/L, posaconazole; 8-0.001 mg/L and fluconazole; 256-0.016 mg/L.
   Generating 1125 MICs in total.

**Data-management:**

1. Determination of modal MIC, $MIC_{50}$, $MIC_{90}$ and range
2. Comparison to previously presented data (ref.) for APX001A for the five most common *Candida* species.

## Results

### Activity of APX001A against *C. auris*

APX001A displayed potent *in vitro* activity against the clinical *C. auris* isolates with modal MIC, $MIC_{50}$, $MIC_{90}$ and range of 0.016 mg/L, 0.016 mg/L, 0.03 mg/L and 0.001-0.125 mg/L, respectively. For the control strains, the MICs were 0.004 mg/L, 0.03 mg/L and 0.06 mg/L. On a mg/L basis, APX001A was the most effective antifungal tested. The $MIC_{50}$ for posaconazole was one dilution step higher (0.03 mg/L) followed by the $MIC_{50}$ for the remaining comparators anidulafungin, micafungin, isavuconazole and itraconazole the (0.125 mg/L), voriconazole (0.5 mg/L), amphotericin B (1 mg/L), and fluconazole (256 mg/L).

### Comparison to other *Candida* species

*C. auris* was as susceptible to APX001A as the most common *Candida* species ($MIC_{50}$ within ±2 dilutions). Thus, the $MIC_{50}$ values were as follows for comparison: *C. albicans* 0.008 mg/L (range 0.001-0.03 mg/L); *C. dubliniensis* $MIC_{50}$ 0.004 mg/L (range 0.002-0.03 mg/L); *C. glabrata* $MIC_{50}$ 0.06 mg/L (range 0.008-0.25 mg/L); *C. parapsilosis* $MIC_{50}$ 0.03 mg/L (range 0.008-0.03 mg/L); and *C. tropicalis* $MIC_{50}$ 0.008 mg/L (range 0.004-0.125 mg/L).

**Table.** MICs of APX001A and comparator antifungals against 122 clinical *C. auris* isolates. The $MIC_{50}$ is highlighted in bold and the modal MIC is underscored. Off-scale MICs are shown as the first concentration outside the tested range.

| | 0.001 | 0.002 | 0.004/<0.008 | 0.008 | 0.016 | 0.03 | 0.06 | 0.125 | 0.25 | 0.5 | 1 | 2 | >2/4 | 8 | 16 | 32 | 64 | 128 | 256 | >256 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **APX001A** | 4 | 6 | 11 | 16 | **41** | 38 | 5 | 1 | | | | | | | | | | | | |
| **AMB** | | | | | | | | | | 14 | **108** | | | | | | | | | |
| **Ani** | | | | | 1 | 12 | 34 | **30** | 12 | 12 | 11 | 2 | 8 | | | | | | | |
| **Mic** | | | | | | 5 | 30 | **69** | 10 | | | | 8 | | | | | | | |
| **Flu** | | | | | | | | | | | 1 | | | | 4 | 10 | 6 | 14 | **33** | 54 |
| **Isa** | | | 20 | 1 | 1 | 19 | 9 | **19** | 21 | 21 | 6 | 5 | | | | | | | | |
| **Itr** | | | 2 | 2 | 9 | 5 | 14 | **34** | 36 | 19 | 1 | | | | | | | | | |
| **Psc** | | | 17 | 5 | 19 | **34** | 32 | 11 | 3 | 1 | | | | | | | | | | |
| **Vor** | | | 1 | | | 1 | 1 | 16 | 13 | **34** | 38 | 13 | 5 | | | | | | | |

## Conclusions

APX001A, the active moiety of the new antifungal compound APX001, shows excellent *in vitro* activity suggesting it may be a promising therapeutic agent against *C. auris* for which options are few.


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**Reference:** Poster P322 presented at TIMM 2017 (doi: 10.1111/myc.12667)