able to inhibit 100% (PhSe)2, AmB and NikZ, or 50% (FCZ, MYC, and CSP) of the fungal growth. Interaction between the drugs was classified as strong synergism when FICi <0.5, weak synergism when 0.5 <FICi <1, additive when 1 <FICi <2, indifferent when FICi = 2, or antagonistic when FICi >2.

Results: (PhSe)2 and NikZ alone were unable to inhibit *C. auris* even by the higher concentrations tested (32 μg/ml and 64–128 μg/ml, respectively). An additive effect of (PhSe)2 was detected with MYC against 30% of the isolates, however, its combination with AmB was antagonistic against all of the isolates, as well as against one isolate with FCZ. All of the other interactions with (PhSe)2 were indifferent. In contrast, NikZ showed strong or weak synergism in association with CSP, AmB, FLU and MYC against 100%, 90%, 30% and 14% of the *C. auris* isolates tested, respectively. An additive interaction of NikZ was also detected with MYC against 86% of the isolates. No antagonistic effect was detected in the combination of NikZ with the antifungals tested.

Conclusion: Although (PhSe)2 seems to not have potential as a future anti-*C. auris* drug, NikZ showed a productive avenue for further studies, mainly in combined therapy against this pathogen.

P076

The promising antimycotic activities of a novel cyclic antifungal lipopeptide against Human Dermatophyte Isolates

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Poster session 1, September 21, 2022, 12:30 PM - 1:30 PM

Objectives: To determine the minimum inhibitory concentrations (MICs) of a novel antifungal lipopeptide against clinical isolates of dermatophytes of human origin.

Methods: To perform antifungal susceptibility testing (AFST) by CLSI microbroth dilution method, a reversed-phase high-performance liquid chromatography (RP-HPLC) purified lipopeptide of 1071.4 Da from a wild-type soil isolate Bacillus subtilis was used and compared with the standard allylamine terbinafine MICs. Briefly, 1200 ml of cell-free culture supernatant was extracted using a solvent mixture and silica gel (230-400 mesh size)-based adsorption chromatography. The semi-preparative RP-HPLC system consisted of an Agilent quaternary pump and a variable wavelength detector equipped with a Phenomenex Luna C18 column (10 mm × 250 mm, 5 μm). The solvent system for RP- HPLC was (A) water with 0.1% trifluoroacetic acid (TFA) and (B) acetonitrile containing 0.1% TFA. The gradient of solvent B used for purification was as follows: 0%-54% for 0-20 min at the flow rate of 1 ml/min, 54%-60% from 20-48 min at 0.5 ml/min, 60%-100% from 48-58 min at 0.5 ml/min, 100%-0% from 58-65 min at 1 ml/min and monitored at 210 nm.

Results: Superficial skin infections are caused by dermatophytes including *Trichophyton* spp. Nowadays, resistance to terbinafine in Trichophyton spp. isolates with higher MICs have been documented in India. We report here the antifungal prowess of a novel small antifungal lipopeptide against 20 clinical isolates of *Trichophyton* spp. of human origins (from human skin scrapings and nails) with the clinical diagnosis of tinea corporis/cruris and tinea unguium. The representative photographs of *T. tonsurans*, *T. rubrum*, and *T. mentagrophytes* complex are provided below. A total of 6 isolates of *T. mentagrophytes* and *T. rubrum* carry point mutations at F397L of squalene epoxidase (SQLE) protein. The *in vitro* antifungal efficacies determined by AFST revealed that the lipopeptide showed less or equivalent MICs (100% inhibition) in the case of five dermatophytes. The lipopeptide drug has exhibited improved MICs against two *T. mentagrophytes* complex and two *T. rubrum* isolates with amino acid substitution F397L in SQLE protein. *Trichophyton mentagrophytes* complex and *T. rubrum* with F397L mutations were inhibited at MICs 4-32 μg/mL of terbinafine. In comparison, the lipopeptide showed 4-16 μg/ml (100% inhibition). In the case of all four Trichophyton tonsurans, the MICs ranged between 2-4 μg/ml for the lipopeptide.

Conclusions: The broad-spectrum lipopeptide showed promising antifungal activity against dermatophytes and may be considered for nano-emulsion formulation and tested for topical application in a mice model.

P077

Detection of CYP51A mutations in airborne *Aspergillus* spp isolates from intrahospital environments

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Introduction: Aerobiological studies have found an increasing number of fungal taxa in the intrahospital environments, including *Aspergillus* species. There is a gap in knowledge on drug-susceptibility in spores circulating in intrahospital environments. In this work, we evaluated the CYP51A genome alterations and *Aspergillus* spore susceptibility to antifungal drugs.

Objectives: To determine the sequence of CYP51A gene in clinical and environmental *Aspergillus* spp. isolates from intrahospital environments in Medellín, Colombia II. To evaluate the phenotypical response of *Aspergillus* isolates harboring mutations in CYP51 gene from intrahospital environments.

Methods: We used *Aspergillus* spp. collected from air and surfaces from intrahospital environments, as well clinical samples. We performed Whole Genome Sequencing (WGS) using HiSeqXten Illumina platform for species identification. Genomes were assembled de novo using the SPADES algorithm. Genome annotation by ab initio prediction was done using the Augustus program. We extracted the sequences from the CYP51A gene and its promoter using OrthoFinder workflow. To identify previously described mutations related with drug-resistance, we performed SNPs search in Geneious software using Clustal Omega. For the determination of broth dilution minimum inhibitory concentrations (MIC) of antifungal agents, we used the Eucast method 9.4.

Results: We identified 26 *Aspergillus* from Fumitagi section using morphological characteristics. Three were isolates from clinical samples and twenty-three were obtained from intrahospital environments. We performed whole genome sequence for identification to species level. We identified 26 *Aspergillus fumigatus* using an in-house script base in BLASTn algorithm for 4 genes: internal transcribed spacer, b-tubulin, calmodulin, and RNA polymerase II. OrthoFinder workflow was performed to obtain CYP51A sequence. Clustal-Omega analysis showed two SNPs A1147G and T11167A, which constituted two non-synonymous mutations N248K and I242V respectively. A total of 8 and 3 isolates presented the changes in the CYP51A gene respectively. To determine their role in antifungal resistance, the strains were tested against 10 concentrations (0.03-8 mg/l) of voriconazole antifungal agent. We used one clinical isolate without genomic changes in the CYP51A gene as control. The MIC was 0.5 mg/l for all the tested isolates. This value suggests isolates are susceptible to voriconazole.

Conclusions:

- Identification of *Aspergillus fumigatus* to species level was achieved through whole genome sequence.
- Described mutations had been related to resistance to voriconazole, itraconazole and had not been tested for posaconazole. In this work, isolates presenting non-synonymous mutations were susceptible to voriconazole with breakpoints >1 mg/l. It is necessary to evaluate the antifungal susceptibility to other antifungal agents.
- The mutation N248K was previously described only in isolates from clinical samples. Mutation I242V was found in clinical and environmental samples from agricultural lands. Here we described SNPs in isolates from intrahospital environments.

This work is the first one describing mutations and elucidating their role in the drug-resistance of airborne *A. fumigatus* in Medellín, Colombia.

Trichophyton tonsurans ***Trichophyton rubrum*** ***Trichophyton mentagrophytes* complex**