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sequences were modelled using the aMD simulation technique and compared with the MIC-test results to correlate folded peptaibol dynamics affected by their amino-acid content and sequence length to their expressed bioactivity. The established relationships between structural characteristics and bioactivity will lead to effective selection of peptaibiotic intervention potentially applied for plant disease management.

POSACONAZOLE IN VITRO AND IN VIVO EFFICACY AGAINST FOUR *CANDIDA AURIS* CLADES

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Candida auris is a multidrug-resistant fungus. In most of the cases the echinocandins are the first line drugs in case of invasive *C. auris* infections. However, triazoles also prove to be effective. We compared daily 6 mg/kg of posaconazole efficacy in a neutropenic murine bloodstream infection model against 10 isolates representing four *C. auris* clades (South Asian n = 2; East Asian n = 2; South African n = 2; South American n = 4; two of which were of environmental origin). As a result of the time-kill assay, it can be stated that posaconazole is a strong antifungal static agent against *Candida auris*. Five days of posaconazole treatment significantly increased the survival rates in mice infected with all of the isolates. The most effective was against the East-Asian clade and the least effective was against the isolates derived from Israel (South American clade). Posaconazole treatment regardless of clades decreased the fungal burden in mice by four orders of magnitude in the kidney and the heart ($P<0.001$) and one order of magnitude in the brain ($P<0.001$). The histopathological examination in posaconazole-treated mice confirmed our results revealing small aggregates of yeast cells in the kidneys and hearts, and in the cerebra and cerebelli. Our data showed that regardless of lethality and fungal tissue burden experiments posaconazole is highly effective in a neutropenic murine model against the four major *C. auris* clades.

BACTERIOPHAGE-MEDIATED BIOCONTROL AGAINST *XANTHOMONAS ARBORICOLA* PV. *JUGLANDIS*

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The genus *Xanthomonas* includes a wide range of plant pathogens varying in host specificity and host interaction. Our research focuses on the walnut blight caused by *Xanthomonas arboricola* pv. *juglandis* (Xaj), one of the most frequent infective diseases of walnut, resulting in serious economic losses. Nowadays, the effectiveness of methods of protection against Xanthomonads infections does not exceed 70%. Currently, copper spray, dithiocarbonate, is most often used to stop the disease. A new European Union law prohibits the routine use of antibiotics in agriculture from 2005, so antibiotics cannot be a temporary solution either. Bacteriophage-based biocontrol can be a promising solution to stop and/or prevent *Xanthomonas* bacteriosis. Importantly, bacteriophages can be used in bioproduction. Ten novel bacteriophages were isolated from soil samples taken under infected walnut trees. We have collected 35 samples from Hungary, and 5 samples from Transylvania. Six isolated polyvalent bacteriophages were chosen for further characterization including their morphological, physiological and genomic analyses. Plaque morphology showed clear plaques referring to a possible strict lytic lifecycle. Transmission electron microscope tests were also performed for morphological characterization. A possible strict lytic lifecycle was also confirmed by genome sequencing, where complete genomes of the novel bacteriophages were determined. We performed multimode reader examinations, so we present also efficacy study results tested on ten Xaj strains. All tested bacteriophages were effective against the tested host bacterium, which could be strengthened when bacteriophages were used in a cocktail. As a result of the host specificity tests, we could conclude that the examined bacteriophages belonged to the broad host specificity group. A significant reduction in symptoms was observed on different *Juglans regia* varieties following phage application compared to the control in a field trial using a bacteriophage cocktail containing six bacteriophages. Based on our results, bacteriophage-based biopesticides can provide an effective tool for the biocontrol of *X. arboricola* pv. *juglandis*.

THE EFFECT OF CASPOFUNGIN IN COMBINATION WITH POSACONAZOLE AGAINST ECHINOCANDIN SUSCEPTIBLE AND RESISTANT *CANDIDA AURIS* ISOLATES

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Candida auris is an emerging potentially multi-resistant pathogen causing invasive infections and nosocomial outbreaks worldwide. It has been published more than 90% and 30% of the isolates are resistant to fluconazole and amphotericin B, respectively; furthermore, the resistance to echinocandins is emerging in the isolates in several countries. For example, an alarming 37% resistance rate to caspofungin was reported in a multicenter analysis derived from India. In this study, the in vitro interaction of caspofungin was determined in combination with posaconazole against echinocandin susceptible (FKS wild type) and resistant (FKS mutant) *C. auris* planktonic and sessile isolates. In case of planktonic cells turbidimetry-based chequerboard microdilution was used for susceptibility testing. For one-day-old biofilms, antifungal susceptibility was evaluated using the XTT colorimetric assay-based chequerboard microdilution method. Drug-drug interactions were assessed utilizing the fractional inhibitory concentration indices (FICIs) and fluorescent microscopy. Median planktonic minimum inhibitory concentrations (pMIC) of *C. auris* isolates to caspofungin ranged 0.5–1 mg L^{-1} and 2– >2 mg L^{-1} for echinocandin susceptible and resistant strains, respectively. In case of posaconazole the median pMICs were between 0.06 and >0.25 mg L^{-1}. In case of one-day old biofilms, MIC values (sMIC) were >32 mg L^{-1} regardless of echinocandin susceptible and resistant phenotype. The sMICs for caspofungin and posaconazole in combination showed 8-128-fold and 4–256-fold decreases, respectively. In addition, caspofungin in combination with posaconazole showed synergistic interaction in case of all sessile isolates tested (median FICI range 0.033–0.375), which was further confirmed the synergy volume ranges calculated by Bliss independence model. The results obtained by statistical interaction analyses correlated well with the fluorescent LIVE/DEAD viability assay. LIVE/DEAD viability staining revealed that caspofungin-exposed wild type and FKS-mutant *C. auris* biofilms exhibited increased cell death in the presence of posaconazole compared to untreated biofilms, caspofungin-exposed sessile populations or posaconazole treated biofilms. The present study is the first analysis evaluating the interaction of an echinocandin and posaconazole against *C. auris* biofilms. We have shown that posaconazole is capable of causing a synergy in combination with caspofungin against *C. auris* especially against biofilms. Our results support the simultaneous use of posaconazole and caspofungin for the treatment of *C. auris* related infections.

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ERGOSTEROL BIOSYNTHESIS AND AZOLE RESISTANCE IN *MUCOR LUSITANICUS*

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Mucoromycota fungi include several opportunistic human pathogenic fungal species (e.g. *Mucor circinelloides* and *Rhizopus oryzae*), which can cause fatal systemic infections in immunocompromised patients, called as mucormycosis. There are some risk factors associated with fungal infections, such as diabetic ketoacidosis and immunosuppressive drug- or corticosteroids treatments. Mucoromycota species are generally resistant to the majority of the routinely used antifungal drugs, such as azoles. The main target of azoles is the lanosterol demethylase (Cyp51/Erg11), which play an important role in the ergosterol biosynthesis of fungi. Ergosterol is an important component of the fungal cell membrane. In addition to the Cyp51/Erg11, other enzymes (Erg6, Erg3, Erg11) of the ergosterol biosynthesis pathway may also participate in the azole resistance. The main goal of this study was to investigate the ergosterol biosynthesis pathway and its role in the azole resistance of *M. lusitanicus*. Relative transcript level of 10 ergosterol biosynthesis specific genes (e.g. *erg2*, *erg3*, *erg6*, *erg7*, *erg24*, and *erg25*) was analyzed using quantitative real-time PCR, after posaconazole treatment. The relative transcription level of certain genes significantly increased after posaconazole treatment. Genome of *M. lusitanicus* encodes three sterol C-24 methyltransferase genes (*erg6a*, *erg6b* and *erg6c*), which catalyzes the conversion of zymosterol to fecosterol and it plays a role in the alternative ergosterol biosynthesis pathway in yeast. Furthermore, in *Cryptococcus neoformans*, Erg6 plays role in growth at high temperature and virulence. We have started to create *erg6* single and double knockout mutants using a CRISPR-Cas9 system. Growth ability, sterol content and sensitivity to azoles of the mutants were examined. The lack of erg6a resulted decreased ergosterol content and growth ability and increased sensitivity to azoles. An in vivo survival test was performed in *Galleria mellonella* and the virulence of MS12-*Δerg6a* strain significantly decreased. No changes were observed in MS12-Δ*erg6b* and MS12-Δ*erg6c* compared to the control strain under the previously tested conditions. The sterol content in the mutant strains was analysed by LC-MS. Ergosterol, zymosterol and eburicol levels were decreased in MS12-*Δerg6a* strain. Our results suggested that Erg6 play important role in the main ergosterol biosynthesis pathway and in the alternative pathway as well. However, in MS12-*Δerg6a* strain the 7-dehydrodesmosterol content significantly increased. We assumed that the lack of erg6a activates a second alternative biosynthetic pathway from zimosterol to 7-dehydrodesmosterol.