P032
Synthetic effect of deformines combined with flucloxacillin against flucloxacillin-resistant Candida Spy. through inhibited Ca^2+ MAPK signaling pathway

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Poster session I, September 21, 2022, 12:30 PM - 1:10 PM

Objectives: The opportunistic fungal infections represent an increasing threat to humans with the increase of immuno-compromised patients, in which Candida albicans is the most common fungal pathogen. Though flucloxacillin (FCA) is still the first line choice to C. albicans infections, several limitations such as increasing drug resistance compromised its clinical application. This study proposes a combination therapy of deformines and FCA to overcome C. albicans resistance.

Methods: Checkerboard microdilution assay was used to determine the minimum inhibitory concentration (MIC) of FCA used alone and in combination with FCA-resistant Candida Spy. Spot assay and disk kill curve was used to investigate the cell viability and dynamic inhibitory effect. Hybrid formation was performed to determine the underlying mechanism of FCA.

Results: A new model of ca^2+ biosignature was established in the in vitro synthetic activity of FCA and deformines.

Conclusion: FCA combined with deformines inhibited the transformation of trans-urea through Ca^2+ MAPK signaling pathway, resulting in reduced infectivity and resistance of C. albicans in vitro and in vivo, which may provide a new option for the treatment of ca^2+ resistant candidiasis.

P030
Highly slow-release urea dressing for chronic dermatophytoses

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Objectives: The aim of this research was to make a biocompatible and affordable nanofibrous wound dressing that is able to release urea slowly at the site of chronic superficial fungal infections over time.

Methods: Polymer solution (10%) of poly (acrylamide) (PCL) was prepared in heptane-free medium. HPC were added into the PCL polymer solution at an equal ratio 1:1. The mixture was emulsified in the bioreactor was used with a stirrer to directly etch fibrous urea membranes. Electrospinning was performed at a 27 G-Neddle sprayed at a distance of 16 cm which the injection flow rate of the solution was 0.2 ml/h and 30 kV voltage was applied. The measurements of urea release were performed with HPLC. Antibacterial tests were done on different fungal species and drug assays were done by DIS-1099 on 24 and 25929. The drug release was monitored for 144 h in a human body simulated system (incubator at 37°C, shaking at 30 rpm, and passing the drug through a new filter sheet in PBS).

Conclusion: The PCL nanofibers with TPH apparently decreased by five times (P<0.01). PCL nanofibers successfully inhibited two important fungal species while its toxicity was observed in MTT assay for extraction of 4 weeks. They were able to release TPH slowly over time which makes them suitable for the treatment of chronic superficial fungal infections.

P031
Post-antifungal effect of the combination of a niflumadipine with amphotericin B and flucloxacillin against fluconozil-resistant and susceptible candidiasis

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Objectives: Increase Candida is a life-threatening condition that kills a large number of immunocompromised patients each year. We used post-antifungal effect studies to analyze the activities of niflumadipine against the major diseases, yeast, and RNase in presence of other antifungal drugs. We tested the phenomenon of post-antifungal effects (PFEs) of fluconozil (FCA), amphotericin B (AMB), and niflumadine (FIC) in in vitro and in vivo activity. We investigated the antifungal activity of the combination of FCA with FIC in the Candida albicans strain.

Methods: We used the phenomenon of post-antifungal effects of the (PFEs) of (FIC) in vitro activity. The MIC of the combination was determined by the serial fourfold dilution method. The MIC of the combination of FCA with FIC was 1/4. The MIC of the combination of FCA with FIC was 1/4.

Results: The FCA showed a post-antifungal effect independent of antifungal FIC dilution. The drug loading with FIC was 1/4. The post-antifungal effect of the combination of FCA with FIC was 1/4. The drug loading with FIC was 1/4.

Conclusion: The combination of FCA with FIC is a strong synergistic effect for the treatment of fluconozil-resistant Candida albicans. However, further research is needed at the clinical utility of our findings.

P032 Efficacy of novel azole compounds (ATAF-1 and ATAF-2) against Candida albicans in a murine model of invasive Candidiasis

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Objectives: Candida albicans is the most common cause of nosocomial bloodstream infections and are associated with substantial morbidity and mortality in immunocompromised individuals. However, limited therapeutic approaches against resistant candidiasis are available. The aim of antifungal resistance highlights the urgent need to develop new therapeutic options and novel treatment strategies to combat later infections. A novel compound Arv-1,2,4-trimethyl-5- triazin, fluconazol-alcohol derivative (ATAF-1) has newly described in vitro activity against Candida species, including fluconazol-resistant isolates. The focus of this study was to evaluate the in vivo effectiveness in a murine model of invasive candidiasis due to C. albicans.

Methods: Treatment with ATAF-1 and ATAF-2 significantly decreased the survival of infected mice compared to the control group (1% GMK mice inoculum).

Conclusion: The antifungal action of ATAF-1 and ATAF-2 and their medium survival rates provided no evidence of a difference versus fluconazol. Although there was an obvious fungal load (mean log CFU of tissue) decrease by ATAF-1 and ATAF-2 in the kidney, spleen, and liver of the treated mice in comparison with the control group and not similar to each other in neck, fluconazol showed a significant decrease in the number of fungal loads, similar to that group treated with ATAF-1 and ATAF-2. Nevertheless, the results of this study indicate that the use of ATAF-1 and ATAF-2 as a therapeutic agent cannot significantly improve in vitro and in vivo antifungal effects against C. albicans, increasing animal survival and significantly decreasing fungal loads.

Conclusion: Although we have identified two new compounds, ATAF-1 and ATAF-2, as novel promising Candidates for the treatment of Candida albicans, more studies of ATAF-1 and ATAF-2 action and their activity in animal models are warranted to understand our enhancement and establish their efficacy.