Symptomatic effect of deferasirox combined with fluconazole against fluconazole-resistant Candida Ssp. through inhibiting Cak1 MAPK signaling pathway

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

Objective: The opportunistic fungal infections represent an increasing threat to humans with the increase of immunocompromised patients, in which Candida albicans is the most common fungal pathogen. Though fluconazole (FCZ) is still the first line choice to C. albicans infections, several limitations such as its increase in drug resistance compromised its clinical application. This study proposes a comparative investigation using deferasirox (DS) and FCZ to overcome C. albicans resistant strains. Methods: Checkerboard microdilution assay was used to determine the minimal inhibitory concentration (MIC) of DS and FCZ alone and in combination with FCZ against Candida Ssp. Spot assay and tray killing curves were used to investigate the cell viability and dynamic inhibitory effect. Hypothalamic formation was performed to ascertain the underlying mechanism of DS. Then, a marine model of candida candida was established to explore the in vivo synergistic activity of DS and FCZ. Results: DS combined with FCZ showed synergistic antifungal activity against FCZ-resistant C. albicans, with a fractional inhibitory concentration index (FICI) of 0.25. Moreover, DS combined with FCZ significantly inhibited the activity of C. albicans cells, which was superior to antagonistic drug drugs. The spot assay and tray killing curve indicated that DS can turn the fungicidal activity of FCZ into fungicidal activity. Hypothalamic formation study showed the inhibitory effect of C. albicans. DS combined with FCZ also significantly inhibited the expressions of Cak1 MAPK signaling pathway-related genes (Ephk1 and CPH) and adhesion-related genes (ALS1). In vivo data showed DS combined with FCZ significantly reduced the portal, CFU numbers, and inflammatory cell infiltration of skin tissue. Conclusion: Our results suggest that DS combined with FCZ inhibited the transformation of yeast through Cak1 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 candida candida.

Highly relevant steal syndrome dressing for chronic non-infected ulcers

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Objective: The aims of this research was to make a biocompatible and affordable nanofibrous wound dressing that is able to release substitude at the site of chronic superficial fungal infection over time. Methods: Polymer solution (10%) of poly (l-lactic acid) (PLA) was prepared in hexafluoro propylene (HFP). The poly (l-lactic acid) (PLA) was dissolved in tetrahydrofuran (THF) solution that has a weight ratio of 1:5. Then the solution was mixed with incorporated ferulic acid. Electrospinning was performed with a 27-Gauge nozzle spraying at a distance of 15 cm which the injection flow rate of the solution was 0.2 ml and a 30 kV voltage was applied. The measurements of drug release were performed with HPLC. Antifungal trial were done on three different fungal species and also drug assay was done by ISO-10993 on 24 and 529 S29. The drug release was monitored for 144 in a human body simulated system (incubation at 37°C, shaking at 30 rpm, and passing the drug through a new Wicomic fiber into PBS). Results: The mean diameter of fibers was diluted at 1242±5 mm for PLA nanofibers without THF and 249±5 mm for PLA nanofibers with THF. The drug loading capacity of PLA was 8% and 15% for PLA with and without THF. The drug loading capacity of PLA with THF was 12% for C. albicans, 8% for C. auris, and 4% for C. tropicalis. Conclusion: The drug release of PLA nanofibers with THF apparently decreased by five times (P<0.01). PLA nanofibers successfully inhibited two important fungal species while no toxicity was observed in MIT assay for extraction of 24 weeks. They were able to release THF daily over time which make them suitable for the treatment of chronic fungal superficial infections.

Post-antifungal effect of the combination of a niludanil fungicide with fluconazole and fluconazole susceptible and resistant Candida albicans

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Objective: 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 activity of synthetic antifungal drug, niludanil (Phytofungicides montepagroyloxy, a xaphoriph (Aspergillus, amature), and a yeast (Candida albicans). The trehalase, hydroxyl-keto, and choline-diesterase C. albicans inhibited the growth of T. mentagrophytes and A. Paragaeum but did not inhibit C. albicans and P. nyssa. None of the samples showed crotic effect after 24 and 2 weeks. Conclusion: The diameter of C. albicans nanofibers with THF apparently decreased by five times (P<0.01). PLA nanofibers successfully inhibited two important fungal species while no toxicity was observed in MIT assay for extraction of 2 weeks. They were able to release THF daily over time which make them suitable for the treatment of chronic superficial fungal infections.

Efficiency of new azole compounds (ATAF1 and ATAF2) against Candida albicans in a marine model of invasive Candidiasis

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Objective: Candida albicans is the most common cause of nosocomial bloodstream infections and are associated with substantial mortality and morbidity in immunocompromised individuals. However, limited therapeutic approaches against invasive candidiasis are available. The in vitro antifungal resistance highlights the urgent need to develop new therapeutic options and novel treatment strategies to counter later infections. A novel compound Aryl I-2,6-4 H2N=CH-5 - triazol- 5-fluoroalkanol- alcohol, axil-3 has newly identified in vitro antifungal activity against Candida species, including fluconazole-resistant isolates. The objectives of this study was to further evaluate the in vitro effectiveness in a marine model of invasive candidiasis due to C. albicans.

Methods: Treatment with ATAF1 and ATAF2 significantly increased the survival of infected mice compared to the control group (1% DMSO plus saline).

Results: The antifungal action of ATAF1 and ATAF2 and their median survival time provided no evidence of a de-

influence between fluconazole. Although there was an obvious fungal load (mean log CFU) of mice decreases by ATAF1 and ATAF2 in the kidney, spleen, and liver of the treated mice in comparison with the control group and not similar to each other in most of the fungal, fluconazole showed a decrease in the number of fungal loads, similar to the group treated with ATAF1 and ATAF2. Nevertheless, the results of this study indicate that the use of ATAF1-1 and ATAF2 as a therapeutic agent can significantly affect 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, ATAF1 and ATAF2, as novel promising Candidates for the treatment of Candida infections, more studies of ATAF1 and ATAF2 action and their antifungal activity are warranted to understand our enhancement and establish their efficacy.