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 fluconazole (FCZ) is still the first line choice to treat C. albicans infections, several limitations such as its increase in drug resistance compromised its clinical application. This study proposes a new treatment strategy of drug delivery platform and FCZ to overcome C. albicans resistance.

Methods: Checkboard microalgal assay was used to determine the minimum inhibitory concentration (MIC) of DFO used along with the combination with FCZ against C. albicans Candida Sep. Spot assay and time-kill curves were used to investigate the cell viability and dynamic inhibitory effect. Hyphal formation was performed to immunoblot the underlying mechanism of DFO. Then, a marine model of cutaneous candidiasis was established to explore the in vivo synergistic activity of DFO and FCZ.

Results: DFO combined with FCZ showed synergistic antifungal activity against FCZ-resistant C. albicans, with a fractional inhibitory concentration index (FICI) of 0.2. Moreover, DFO combined with FCZ significantly inhibited the activity of C. albicans cells, which is superior to amphotericin B. The spot assay and time-kill curve assay indicated that DFO can turn the fungicidal activity of FCZ into fungicidal activity. Hyphal formation study showed the inhibitory effect of C. albicans. DFO combined with FCZ also significantly inhibited the expression of C. albicans MAPK signaling pathway-related genes (CEK1 and CPH1) and adhesion-related genes (ALS1). In vivo data showed DFO combined with FCZ significantly reduced the portal, CFU number, and inflammatory cell infiltration of skin tissue.

Conclusion: Our results suggest that DFO combined with FCZ inhibited the transformation of yeast through Cek1 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 cutaneous candidiasis.

P020
Highly sensitive release wound dressing for chronic dermatophytosis

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3Poster session, 2022, 12:30 PM - 1:10 PM

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

Methods: Polymer solution (10%) of poly (acrylamide) (PCL) was prepared in hexadecyltrimethylammonium (HDTMA) solution. The pH of the solution was adjusted to 5% for drug-loaded samples. Electrospinning was performed with a 27-G needle-sprayed at a distance of 14 cm which the injection flow rate of the solution was 0.2 ml and 30 kV voltage was applied. The measurements of drug release were performed with HPLC. Antifungal tests were done on different fungal species and antifungal test was done by son-D0399 on 49 and 5299F. The drug release was monitored for 144 h in a human body simulated system (incubation at 37°C, shaking at 50 rpm, and passing the drug through a filter with 0.2 micron size into PBS).

Results: The mean diameter of fibers was obtained at 1024 nm for PCL nanofibers without TPH and 249 nm for PCL nanofibers with TPH. The drug loading capacity was 4.5% for drug-loaded samples. Electrospinning was performed with a 27-G needle-sprayed at a distance of 14 cm which the injection flow rate of the solution was 0.2 ml and 30 kV voltage was applied. The measurements of drug release were performed with HPLC. Antifungal tests were done on different fungal species and antifungal test was done by son-D0399 on 49 and 5299F. The drug release was monitored for 144 h in a human body simulated system (incubation at 37°C, shaking at 50 rpm, and passing the drug through a filter with 0.2 micron size into PBS).

Conclusion: The diameter of PCL nanofibers with TPH apparently decreased by five times (/> 0.1). PCL nanofibers successfully inhibited two important fungal species while no toxicity was observed in MTSS for extraction of 3 weeks. They were able to release TPH slowly over time which make them suitable for the treatment of chronic superficial fungal infections.

P021
Post-antifungal effect of the combination of a nifurtimox-lactophenol with amphotericin B and fluconazole for fungocandidiasis-susceptible and resistant Candida albicans

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

Objectives: Incure 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 medicines in the chronic/acute Candida albicans, amphotericin B (AmB), fluconazole (FLC), and nifurtimox-lactophenol (ATF) as a new combination for the treatment of Candida albicans in cases of the absence of the effectiveness of FLC and/or AmB.

Methods: We studied the phenomenon of post-antifungal effects (PAE) of fluconazole (FLC), amphotericin B (AmB), nifurtimox-lactophenol (ATF), and combinations of FLC + AmB, ATP + AmB, and FLC + AmB + ATP against 17 C. albicans isolates obtained from the Iran Cancer Center patients. The isolates that had been sensitized against AmB and nifurtimox-lactophenol, served as a control group. Colony counts were performed at 0, 2, 4, and 24 after a brief (1 h) antifungal exposure. Results: The FLC had a detectable post-antifungal effect independent of antifungal concentration and dose-related drug (FLC). Drug combinations were performed with fluorescence (CFDA, AmB, and ATP, nucleic acid-binding dye) and, in the case of FLC, using the confocal microscopy images, the alterations in the cellular distribution of fluorescence were assessed. We observed that nifurtimox-lactophenol had a synergistic effect against C. albicans isolates (n = 17).

Conclusion: Our findings suggest that brief exposure to ATP, in combination with FLC and AmB, at low concentrations of the medicines utilized, could be effective in the evaluation and optimization of new dosage regimens to manage Candida albicans.

P022
Efficacy of novel azole compounds (ATTAF-1 and ATTAF-2) against Candida albicans in a murine model of invasive Candidiasis

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

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 reinfection candidiasis are available. The main in antifungal resistance highlights the urgent need to develop new therapeutic options and novel treatment strategies to combat later infections. A novel compound 4aryl-1,2,4-triazole-5-thiophene, fluconazole-aldehyde diketopiperazine (ATTAF-A), has newly discovered with potent in vitro activity against Candida species, including fluconazole-resistant isolates. The objective of this study was to further evaluate the in vivo effectiveness in a murine model of invasive candidiasis due to C. albicans.

Methods: Treatment with ATTAF-1 and ATTAF-2 significantly increased the survival of infected mice compared to the control group (p<0.01). Efficacy.

Conclusion: The antifungal action of ATTAF-1 and ATTAF-2 and their median survival times proved to reduce the effectiveness of fluconazole-resistant fungi. Although there was an obvious fungal load (mean log CFU of tissue) reduction by ATTAF-1 and ATTAF-2 in the kidney, spleen, and liver of the treated mice in comparison with the control group and not similar to each other in median fungal load, fluconazole showed a decrease in the number of fungal loads, similar to the group treated with ATTAF-1 and ATTAF-2. Nevertheless, the results of these studies indicate that the use of ATTAF-1 and ATTAF-2 as a therapeutic agent can 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, ATTAF-1 and ATTAF-2, as novel promising Candida for the treatment of Candida infections, more studies of ATTAF-1 and ATTAF-2 action and their mechanism of action are concluded to warrant our understanding and establish their efficacy.