OBJECTIVES: 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 (FCA) is still the first line treatment for C. albicans infections, several limitations such as an in-dose resistance to compromised clinical application in patients with severe recurrent infections. This study proposes a combination therapy of antifungal agents and FCA to overcome C. albicans resistance.

METHODS: Checkerboard microdilution assay was used to determine the minimum inhibitory concentration (MIC) of FCA. DFO used alone or in combination with FCA against 158 C. albicans isolates. Spore preparation and thin-layer agar plates were used to investigate the cell viability and dynamic inhibitory effect. Hybridization was performed to ascertain the underlying mechanism of DFO. Then, a marine model of candidiasis was established to explore the in vivo antifungal activity of DFO and FCA.

RESULTS: DFO combined with FCA showed synergistic antifungal activity against FCA-resistant C. albicans, with a fractional inhibitory concentration index (FICI) of 0.22. Moreover, DFO combined with FCA significantly inhibited the activity of C. albicans, which is resistant to antifungal drugs. The spot assay and thin-layer agar plates indicated that DFO could turn the fungicidal activity of FCA into fungicidal activity. Hybridization study showed the inhibitory effect of C. albicans. DFO combined with FCA also significantly inhibited the expression of Cdc2 MAPK signaling pathway-related genes (CEK1 and CPH1) and adhesion-related genes (ALS1). In vivo data showed DFO combined with FCA significantly reduced the portal, CPU numbers, and inflammatory cell infiltration of skin tissues.

CONCLUSION: Our results suggest that DFO combined with FCA inhibited the transformation of yeast through Ca2+ 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 candidiasis.

P030
High-low release antifungal wound dressing for chronic dermatophytosis
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Poster session 1, September 21, 2022, 12:30 PM - 1:30 PM

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

METHODS: Polymer solution (10%) of poly (acrylamide) (PCL) was prepared in heparinized saline-sodium (HSSP). Turbidimetric assay was done with a concentration of 5% for drug-loaded samples. Electrospinning was performed at a 27-G needle-shaped syringe at a distance of 14 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. Antimicrobial assays were done on three different fungal species and MIT assay was done by ISO-19994 on 24 and 529 mp. The drug release was monitored for 144 h in a human body simulated system (incubation at 37°C, shaking at 10 rpm, and passing the drum through a wet filter-sterilized filter bed). In order to perform this route, the syringe was filled with 2 ml of 24-kpa filtrate, and the needle tip was positioned on the Perspex plate, and the plate was moved back and forth 2 cm 2 times.

RESULTS: The mean diameter of fibers was obtained at 1124 nm for PCL nanofibers without THP and 249 nm for PCL nanofibers containing THP. The drug loading efficiency was 65% for drug-loaded samples. Electrospinning was performed at a 27-G needle-shaped syringe at a distance of 14 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. Antimicrobial assays were done on three different fungal species and MIT assay was done by ISO-19994 on 24 and 529 mp. The drug release was monitored for 144 h in a human body simulated system (incubation at 37°C, shaking at 10 rpm, and passing the drum through a wet filter-sterilized filter bed). In order to perform this route, the syringe was filled with 2 ml of 24-kpa filtrate, and the needle tip was positioned on the Perspex plate, and the plate was moved back and forth 2 cm 2 times.

CONCLUSIONS: The diameter of PCL nanofibers with THP apparently decreased by five times (P < 0.01). PCL nanofibers successfully inhibited two important fungal species while no toxicity was observed in MTT assay for incubation of 4 weeks. They were able to release THP slowly over time which makes them suitable for the treatment of chronic superficial fungal infections.

P031
Post-antifungal effect of the combination of a nifuruloin with amphotericin B and fluconazole against fluconazole-resistant and susceptible Candida albicans
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OBJECTIVES: Increase Candidiasis is a life-threatening condition that kills a large number of immunocompromised patients yearly. We used post-antifungal effect studies to analyze the activities of medications in comparison to their antifungal activity. To employ the antifungal activity and antifungal resistance of C. albicans, we used the synergistic effect of the combination of the mixture of the agents against the reference strains.

METHODS: We tested the phenomenon of post-antifungal effects (PAE) of fluconazole (FCA), amphotericin B (AMB), nifurtulim (NIF), and combinations of FLC + AMB, FLC + NIF, AMB + NIF against 17 C. albicans isolates obtained from Iranian patients suffering from the cancer infections that had been treated with antifungal treatment, served as a control group. Colony counts were performed at 0, 2, 4, 6, and 24 h after a brief (1 h) antifungal exposure. Results: The FLC had detectable post-antifungal effect independent of antifungal concentration and residual drug-free (FCA) control. When all AMB and FLC were compared with FLC alone, significant variations in the post-antifungal effect of the isolate were observed. Combining AMB and FLC resulted in effective activity compared to FLC alone. Combination regimens were more efficient in general. The maximum effect was observed for the NIF + AMB combination, resulting in 96% of the drug still active against the pathogenic strain of Candida albicans (n = 17). Our findings indicate that brief exposure to FLC, in combination with FLC + AMB, at low concentrations of the included antifungals, could be effective in the evaluation and optimization of new dosing strategies to manage multidrug-resistant. However, future research will look at the clinical utility of our findings.

P032
Efficacy of novel azole compounds (ATTAF-1 and ATTAF-2) against Candida albicans in a marine 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 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 combat later infections. A novel compound Arf-1, 2-m, 4-trinitro-5- fytlythiophene alcohol-derivative (ATTAF-1), has newly described its in vivo activity against Candida species, including fluconazole-resistant isolates. The object of this study was to evaluate the in vivo effectiveness in a marine 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 (1% BMDM plus inoculum).

RESULTS: The antifungal action of ATTAF-1 and ATTAF-2 and their median survival times provided no evidence of a differential effect versus fluconazole. Although there was an obvious fungal load (mean log CFU of mice inoculated with 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 its median and 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 this study indicate that the use of ATTAF-1 and ATTAF-2 as a therapeutic agent can significantly improve in vivo and in vitro 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 Candidates for the treatment of Candida infections, more studies of ATTAF-1 and ATTAF-2 and their action mechanisms must be evaluated to understand our effectiveness and establish their efficacy.