

Trans-ungual Delivery of AR-12, a Novel Antifungal Drug

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Purpose

With the growing prevalence of onychomycosis, there is also growing need for more potent and safer drugs for improving the success rate of topical therapy of onychomycosis. The novel antifungal drug AR-12 was found to be highly potent against *T. rubrum* and *T. tonsurans*, the fungal organisms predominantly responsible for causing onychomycosis. The objective of this project was to investigate the inherent ability of AR-12 to penetrate into and across the human nail plate. The second objective was to explore suitable permeability enhancers to improve the trans-ungual delivery of AR-12.

Methods

In vitro permeation studies of AR-12 was performed across the human cadaver nail plates using Franz diffusion cells. Donor and receiver compartments were filled with 0.5 ml of 5% w/v alcoholic drug solution and 5 ml of ethanol and phosphate buffer saline mixture (1:1) respectively. Samples (200 μ l) from the receiver compartments were withdrawn at different time points and the amount drug was analyzed by HPLC. TranScreen-N method was followed to screen the potential permeability enhancers. Then, *In vitro* transport studies of AR-12 with leading enhancers were performed for 7 days.

Results

The amount of drug permeated across the nail plate after one week was 0.82 ± 0.11 ng/cm². The amount of drug retained in active diffusion area of the nail plate was $\sim 0.42 \pm 0.02$ μ g/mg. . TranScreen-N clearly showed that PEG-400 could be a potential enhancer of trans-ungual delivery of AR-12. Furthermore, *in vitro* permeation studies of AR-12 in presence of 10% PEG-400 resulted in 6 folds more enhancement in trans-ungual drug transport compared to control solution. The drug load in the nail plate was found to be 2 folds more in presence of 10% PEG-400.

Conclusion

AR-12 is a promising novel antifungal for the treatment of onychomycosis. AR-12 has been found to penetrate across the nail plate in significant amounts which can be further improved with the use of appropriate permeation enhancer like PEG-400.