## Overcoming the Nail Barrier: Delivering Antifungals through the Nail to Treat Nail Fungus Using a Combination of Physical and Chemical Methods

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Onychomycosis, colloquially referred to as nail fungus, is the fungal infection of the nail. Current options for treatment are oral antifungals, which are associated with potential side effects, and topical formulations, which must permeate through the entire thickness of the nail in order to be effective. Many studies have investigated individually the use of various methods, such as nail abrasion (sanding the nail), chemical permeation enhancement (using chemicals to break down the protein binding that constitutes the "hardness" of the nail), and iontophoresis (application of electrical current to "push" charged drugs through the nail). The purpose of this study was to investigate if the combination of these methods would elicit a synergistic effect, further enhancing drug permeation through the nail barrier. Donated human cadaver toenails from a tissue bank will be mounted onto modified Franz diffusion cells to test different combinations of abrasion, permeation enhancers, and iontophoresis on the permeability of the nail barrier. A terbinafine hydrochloride gel formulation will be put into the donor chamber, and the permeation into the receptor medium will be assessed at various time points to determine the permeation profile of the drug through the nail over time. At the end of the study, the terbinafine content will be extracted from the nails, and high performance liquid chromatography will be used to determine the concentrations of drug present in the samples obtained. As all three methods being tested enhance drug delivery through different mechanisms, it is anticipated that the increase in permeability will be higher than any one or two methods alone. Evaluation of the combined effects of these methods will enhance understanding of delivering drugs through the nail, and will contribute to more efficient topical treatment options for onychomycosis. Funded by the Rutgers University Center for Dermal Research CDR and Changzhou Huajia Medical Device Ltd and NIH R25ES020721 and ORED.

