

Iontophoresis to enhance topical delivery of terbinafine to the nail

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Purpose: Onychomycosis (fungal infections of the nail plate and/or bed) is usually treated with oral antifungals due to the low efficacy of topical therapy. The latter is limited mainly by the very poor permeability of drugs in the nail plate. So far, only a few unguinal enhancers, such as N-acetyl cysteine, mercaptoethanol, N-(2-mercaptoacetyl) glycine, have been identified. Physical techniques to enhance drug permeation into and through the nail plate that have been investigated include low frequency ultrasound, electricity, filing and etching. The aim of this study was to investigate the application of electric current to enhance the unguinal permeation of terbinafine – an antifungal agent that is currently delivered systemically for the treatment of onychomycosis.

Methods: Hydrated bovine hoof membranes (thickness \approx 150-200 μm , used as a model for the nail plate) were sandwiched in Franz diffusion cells and the donor and receptor compartments were filled with drug solution/suspension and a receiver fluid. Electric current (0.2-1 mA) was applied for 1h, after which the experiment was allowed to continue for various durations. At time intervals, the receptor phase was sampled and analysed for drug concentration. At the end of the experiment, the hoof membrane surfaces were cleaned and drug content in the membrane was quantified following extraction.

Results: Greater drug movement into and through the hoof membranes was found upon application of electric current as shown in the Figures below. There was not, however, a direct linear relationship between current density and drug permeation. The nature of the drug vehicle and of the electrode also influenced drug permeation (data not shown). Drug (a small proportion) was also found in the parts of the hoof membranes that were not directly exposed to the drug in the donor compartment of the Franz diffusion cells. This shows that lateral diffusion of drug in the hoof membrane occurred to a certain extent.

Conclusion: Iontophoresis is promising as a technique to enhance unguinal penetration of terbinafine.



