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Hydrosoluble medicated nail lacquers: *in vitro* drug permeation and corresponding antimycotic activity

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Conflicts of interest
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Summary

Background Two nail lacquers, containing ciclopirox (CPX) or amorolfine (MRF), based on water-insoluble polymers are currently considered mainstays of topical treatment of onychomycosis. The present study aimed at evaluating the antimycotic activity of a new water-soluble nail lacquer containing CPX (CPX/sol), easily removable by washing with water and applicable to periungual skin.

Objectives To compare transungual permeation of CPX with that of MRF in the same hydroxypropyl chitosan-based nail lacquer (MRF/sol) and with a nonwater-soluble reference (Loceryl®; Galderma International, La Défense, France), and to evaluate the antimycotic activity of CPX/sol and Loceryl® against the most common fungal strains that cause onychomycosis.

Methods In vitro drug permeation experiments with CPX/sol, MRF/sol and Loceryl® were carried out through bovine hoof slices. Experimental permeates from CPX/sol and Loceryl® underwent in vitro susceptibility testing against clinical isolates of dermatophytes, moulds and yeast.

Results MRF transungual flux from MRF/sol lacquer was significantly higher when compared with Loceryl®. CPX was able to permeate hoof membranes more easily compared with MRF. CPX and MRF concentrations in the subungual fluids collected after application of CPX/sol or Loceryl® were sufficient to inhibit fungal growth, with the exception of *Candida parapsilosis*. Smaller amounts of fluid containing CPX were required for complete inhibition of fungal growth. Efficacy index values were significantly higher for CPX/sol.

Conclusions Application of the CPX/sol nail lacquer allows rapid nail penetration of CPX, providing CPX levels sufficient to inhibit fungal growth for a prolonged period of time (30 h) after application of lacquer dose. CPX/sol nail lacquer appeared superior to the market reference Loceryl® in terms of both vehicle (hydroxypropyl chitosan) and active ingredient (CPX) as witnessed by its higher efficacy on all nail pathogens.

Fungal infection of the nail unit, namely onychomycosis, is a common disorder that is currently treated with broad-spectrum antifungals delivered via systemic and/or topical routes.[1–3] Topical agents penetrate and accumulate in the nail plate, with the highest concentrations found near the surface; the keratinized structure of nails provides a high resistance to drug permeation so that topical monotherapy is currently recommended only for the earlier stages of the disease.[3–5] Systemic antimycotics reach the infection site via the nail bed and the nail matrix thus becoming distributed throughout the nail. However, oral administration of terbinafine or azoles does not always result in cure, and failure may be expected in 25–50% of cases;[1–3] moreover, the risk of serious adverse reactions and drug interactions cannot be excluded.[6]

Recently several reports have described successful combinations of topical and oral antifungals in the treatment of severe onychomycosis.[3,4,7–9] The rationale of combined therapies consists of exploiting synergistic drug activities and/or complementary penetration routes into the nail unit, where each drug alone does not accumulate in sufficient concentrations: oral drugs rapidly reach the nail bed via blood circulation while topical agents penetrate the nail plate and may be effective in preventing reinfection.[10,11]

