An investigation into correlations between onycheal antifungal drug flux and resulting fungal inhibition in *in vitro* assays.

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Onychomycosis (fungal infection of the nail plate and/or nail bed) is currently mainly treated with oral antifungals, and topical therapy is generally only used in mild disease due to its limited success rate. For a topical antifungal preparation to be effective, the drug must partition out of the formulation into the nail plate, diffuse through the latter and reach the nail bed in sufficient quantities and kill the fungus. Thus, in *in vitro* studies to predict the *in vivo* efficacy of topical nail products, the most common measurements are: i) drug concentrations in the nail plate and/or a simulated nail bed, such as agar gel, or, ii) the fungicidal activity of the permeated drug on fungi-seeded agar gels. There have been few investigations in which both drug concentrations in the nail plate, simulated nail bed and the antifungal inhibition have been measured together, in the same experimental setup, and where correlations between drug concentrations and antifungal inhibition have been explored. This was, therefore, the subject of the study reported in this abstract

Methods: 10µl or 10mg of three formulations – A, B and C – of an anti-fungal drug were applied on to the dorsal surface of excised cadaver nail plates (leaving a drug-free zone around the nail edges). The nail plates (thicknesses ~ 0.5mm) were then placed on agar gels seeded with *Trichophyton mentagrophytes* or *T. rubrum* (the most common causative organisms of onychomycosis), with the ventral nail surface contacting the agar gel. The set-up was incubated at 27^{o}C for 7d, after which, i) the diameter of the zone of fungal inhibition around the nail plate, and ii) drug concentrations in the nail plate and in the agar gel were determined. Correlations between fungal inhibition and drug concentrations were explored.

Results and Discussion: The diameter of the zones of fungal inhibition, and drug concentrations in the nail plate and in the agar gel (measured by HPLC) are shown in Table 1. It can be seen that the greatest fungal inhibition zone and highest drug concentrations were achieved with formulation B. Formulations A and C both showed lower drug concentrations and zones of inhibition compared to B, but were similar to each other.

Conclusion: In general, a positive correlation was found between concentration and activity (in terms of fungal inhibition) of drug that had permeated through the nail plate from 3 different formulations.

		Drug-in-nail (inside and outside formulation application area) (mg/g)	**Sum of Drug-in-gel (immediately underneath nail and 3-5mm away) (mg/g)**	**Inhibition zone (mm)**
T. mentagrophytes	A :10% lacquer	0.430±0.414	0.007 ± 0.004	34.3 ± 2.9
	B: 10% Gel	1.30±0.25	0.076 ± 0.080	40.5 ± 1.3
	C: 20% lacquer	0.640±0.414	0.027 ± 0.029	33.0 ± 3.6
T. rubrum	A :10% lacquer	0.365±0.089	0.009 ± 0.002	24.5 ± 0.7
	B: 10% Gel	1.63±0.24	0.081 ± 0.072	31.5 ± 2.1
	C: 20% lacquer	0.403±0.083	0.013 ± 0.012	27.0 ± 1.7