

## Evaluation of different setups for the measurement of drug penetration into the nail

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Topical therapy of onychomycosis, a fungal infection of nail plate and/or nail bed, offers an attractive alternative to treatment with systemic antifungals. To treat fungal infections locally, antifungal-loaded nail lacquers have been prepared in our laboratory. Franz diffusion cells have been used to investigate drug permeation from such lacquers into and through the nail plate *in vitro*. Although Franz diffusion cell is convenient for permeation study, it does not mimic the physiological fungal-infected nail bed conditions for evaluating antifungal effectiveness. Alternative setups to the Franz diffusion cells have been investigated, where the nail plate is placed on a wet cotton ball [1] or on agar gel, the wet cotton ball and agar gel being equivalent to the receptor compartment of Franz diffusion cells, and the drug-loaded vehicle is applied to the surface of the nail plate. Such a setup can allow the permeation of anti-fungal drugs to be tested directly, for example, if the agar gel is seeded with fungi, drug permeation through nail plate and into agar gel could be measured as a fungi-free clearance zone to be directly related to drug penetration into and through the nail plate [2].

The *aim* of this study was to conduct permeation using 3 different setups: Franz diffusion cells, wet cotton ball, and agar gel to investigate whether the same permeation results would be obtained with a nail lacquer formulation. Subsequently, 4 nail lacquers were used in 2 of permeation setups to detect whether the order of best to worst formulation was the same in the different setups.

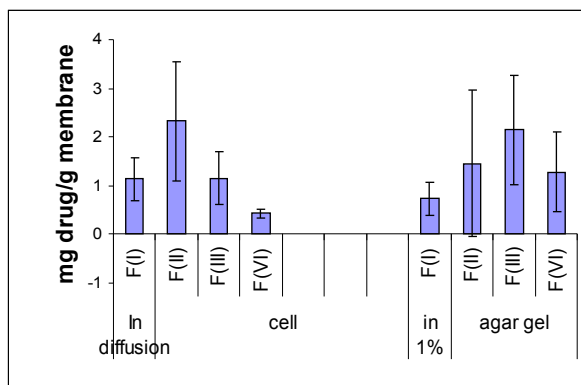
Drug-loaded nail lacquer was applied on the surface of hoof membrane (used as a model of nail plate), which was then mounted in Franz diffusion cells, on wet cotton ball, or on agar gel (0.2, 0.5, and 1% w/v). Permeation studies were conducted at 37°C for 24h. At the end of the experiment, the amount of drug remaining in the lacquer film and that had permeated in the hoof membrane was determined.

Table 1 shows that permeation results of cotton ball and 0.5% agar gel were significantly lower than the others. 0.2 and 1% w/v agar gel and Franz diffusion cells permeation setups gave similar permeation results and there was no statistically significant difference between these 2 setups ( $P>0.05$ ). This shows that 0.2 and 1% agar gel setups could be used instead of Franz diffusion cells. When 4 nail lacquers FI, II, III, and VI were tested using 1% agar gel and Franz diffusion cell, all the formulations gave similar permeation results ( $P>0.05$ , Figure 1). Therefore, it was not possible to determine whether the order best to worst formulation was the same in these studies.

Table 1 Penetration studies of one nail lacquer formulation in different setups (n=3)

Setup	% of applied drug in hoof membrane (Mean ± S.D.)
Franz diffusion cell	5.5 ± 2.4
Cotton wool	1.6 ± 0.2
0.2% agar gel	3.4 ± 2.6
0.5% agar gel	1.0 ± 0.7
1% agar gel	2.3 ± 1.2

Figure 1 Comparison of 4 nail lacquers the different permeation setups (n=6)



1. Hui X *et al.*, *J. pharm. Sci.*, 2002, 91 (1) 189-195; 2. Nakashima T *et al.*, *J. Infect. Chemother.*, 2002, 8(4) 331-335

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