

Keratin Biomembranes

Subjects: Biomaterials

Submitted by:  Marina Nisnevitch

Definition

Difficulties in obtaining human nails that are large enough for examining the penetration of drug formulations led to produce keratin films regenerated from human hair. The structure, surface morphology, chemical characterization and thermal stability of the films were characterized and were compared to those of human nail, hair and bovine hoof samples using SDS-electrophoresis, SEM, XRD, FTIR and TGA. The structure of the obtained films was found to be closer to human nails than to hair or bovine hooves. The keratin films were infected with *Trichophyton rubrum* and were proven to be appropriate for serving as a model for studying onychomycosis.

1. Introduction

More than 10% of the global population is affected by fungal diseases on nail plates and nailbeds, also known as onychomycosis, which are caused mainly by dermatophytes ^[1]. No effective medication of onychomycosis has been proposed to date. Current treatment methods include local and oral drug delivery. Local treatment is preferable, since it has fewer negative impacts on internal organs and can be applied in situ. However, it also has some limitations caused by structural and physical properties of the nail plate, which serves as a barrier to the efficient transport of drugs to the infected site ^[2]. A high rate of drug penetration through the nail plate is a necessary but insufficient condition for successful topical treatment of fungal infections. The total amount of active components needed for effective treatment must also be taken into account ^[2].

2. Models

A model that can be used to evaluate the effectiveness of various drug formulations could make a significant contribution to preclinical and preliminary assessments of drug penetration. Such models have not been developed to date due to low availability of human nail material. For this reason, it is necessary to produce materials that have similar structural and physiological characteristics to human nail plates and can replace them with maximal similarity to *in vivo* tests.

Several models have been proposed for predicting transungual drug absorption into human nail plates ^{[3][4]}. However, these models require individual nail plates, which complicate their widespread use. Other models use membranes based on bovine hooves ^[5]. These models do not provide a close approximation to human nails, since the density of the keratin fibers matrix in bovine hooves is lower compared to the human nail. The low density of the matrix in bovine hooves is due to fewer disulfide bounds compared to human nail plates ^{[6][7]}. As a result, bovine hooves can be less sensitive to factors disrupting disulfide bonds applied to increase the permeability of drugs.

Keratin films made from human hair were proposed for *in vitro* simulations ^{[8][9]}. Sufficient size and flat shape of the prepared membranes enable the application of the drugs to the membrane surface in a uniform manner to study their penetration potential.

The structure of the films was compared to that of human nail plates and bovine hooves using X-ray diffraction analysis (XRD), scanning electron microscopy (SEM), thermogravimetric analysis (TGA) and Fourier transform infrared spectroscopy (FTIR) ^[10]. Properties of the films were found to be much closer to the nail pattern than to hair from which the films were produced or the hoof sample.

The keratin films were infected with the dermatophytic fungus *Trichophyton rubrum* and three days after infection, all films were not only covered superficially by white and cotton-like fungi on the surface, but fungi also penetrated inside and through the films. The keratin films can be used as a substitute for nails in *in vitro* experiments on modelling and treatment of onychomycosis and can replace nail plates in permeation and penetration studies of antifungal drugs ^[10].

References

1. A.K. Gupta; Fiona Simpson; New therapeutic options for onychomycosis. *Expert Opinion on Pharmacotherapy* **2012**, *13*, 1131-1142, 10.1517/14656566.2012.681779.
2. Thomas Colley; Gurpreet Sehra; Leah Daly; Genki Kimura; Takahiro Nakaoki; Yuki Nishimoto; Yasuo Kizawa; Pete Strong; Garth Rapeport; Kazuhiro Ito; et al. Antifungal synergy of a topical triazole, PC945, with a systemic triazole against respiratory *Aspergillus fumigatus* infection. *Scientific Reports* **2019**, *9*, 9482, 10.1038/s41598-019-45890-w.
3. Matthew Traynor; R.B. Turner; C.R.G. Evans; R.H. Khengar; S. A. Jones; M.B. Brown; Effect of a novel penetration enhancer on the ungual permeation of two antifungal agents. *Journal of Pharmacy and Pharmacology* **2010**, *62*, 730-737, 10.1211/jpp.62.06.0009.
4. Dirk Mertin; Bernhard C. Lippold; In-vitro permeability of the human nail and of a keratin membrane from bovine hooves: prediction of the penetration rate of antimycotics through the nail plate and their efficacy.. *Journal of Pharmacy and Pharmacology* **1997**, *49*, 866-872, 10.1111/j.2042-7158.1997.tb06127.x.
5. Dirk Mertin; Bernhard C. Lippold; In-vitro Permeability of the Human Nail and of a Keratin Membrane from Bovine Hooves: Influence of the Partition Coefficient Octanol/Water and the Water Solubility of Drugs on their Permeability and Maximum Flux. *Journal of Pharmacy and Pharmacology* **1997**, *49*, 30-34, 10.1111/j.2042-7158.1997.tb06747.x.
6. Howard P. Baden; Lowell A. Goldsmith; Barbara Fleming; A comparative study of the physicochemical properties of human keratinized tissues. *Biochimica et Biophysica Acta (BBA) - Protein Structure* **1973**, *322*, 269-278, 10.1016/0005-2795(73)90303-6.
7. Robert C Marshall; Jm Gillespie; The Keratin Proteins of Wool, Horn and Hoof from Sheep. *Australian Journal of Biological Sciences* **1977**, *30*, 389, 10.1071/bi9770389.
8. Lusiana; Reichl, S.; Müller-Goymann, C. Keratin film made of human hair as a nail plate model for studying drug permeation. *J. Pharm. Biopharm.* 2011, *78*, 432–440.
9. Lusiana; Reichl, S.; Müller-Goymann, C. Infected nail plate model made of human hair keratin for evaluating the efficacy of different topical antifungal formulations against *Trichophyton rubrum* in vitro. *J. Pharm. Biopharm.* 2013, *84*, 599-605.
10. Anton Valkov; Michael Zinigrad; Alexander Sobolev; Marina Nisnevitch; Keratin Biomembranes as a Model for Studying Onychomycosis. *International Journal of Molecular Sciences* **2020**, *21*, 3512, 10.3390/ijms21103512.

Keywords

keratin films;onychomycosis model;Trichophyton rubrum

Retrieved from <https://encyclopedia.pub/1396>