



Is Rabbit Ear Skin a Good Model for Human Skin for in Vitro Permeation Experiments?

S. Nicoli ¹, C. Padula ¹, P.W. Wertz ², P. Santi ¹

¹ Department of Pharmacy, University of Parma, Italy

² Dows Institute for Dental Research, Iowa State University, Iowa

Introduction

The first step in the evaluation of a new transdermal formulation/molecule is that of in vitro permeation studies. The reference barrier for these studies is human skin, but its limited availability often necessitates the use of other skin models.

Aim

The aim of this work was to characterize rabbit ear skin in order to verify if it is an acceptable model for human skin.

The characterization included:

- histological analysis
- determination of lipid composition
- permeation experiments

Methods

Lipid composition

Pre-weighted pieces of SC were extracted successively for 20 minutes in a sonication bath with chloroform:methanol 2:1, 1:1 and 1:2 v/v. HPTLC lipid separation was performed according to (1-3).

Permeation experiments:

Franz type diffusion cells

Donor: 0.5 ml of nicotinamide water solution (200 mg/ml)

0.5 ml of caffeine saturated water solution (≈20 mg/ml)

0.5 ml of progesterone saturated solution in 0.4 HPβCD water solution (229 μg/ml)

Membrane: rabbit or pig ear skin, isolated pig epidermis

Receptor: saline solution (0.9% NaCl) for nicotinamide and caffeine

saline solution (0.9% NaCl) containing 0.4% of HPβCD for progesterone

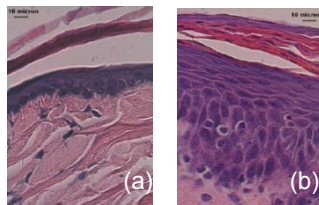
Results

Histology

Thickness (μm±sd) of rabbit, pig, human and mouse skin.

	Rabbit ear	Pig ear	Human	Mouse
Stratum corneum	11.7±1.7	9.1±1.7	12.5	6.7
Viable epidermis	17.0±2.6	61.7±6.7	53.5	9.6
Full thickness	276.4±59.8	1177.1±29.9	nr	nr

The structure and thickness of stratum corneum resulted comparable for pig and rabbit ear skin, whereas the other layers, namely viable epidermis and dermis, were different not only in terms of thickness but also as structure.



Sections of rabbit (a) and pig (b) ear skin (40x)

Lipid composition

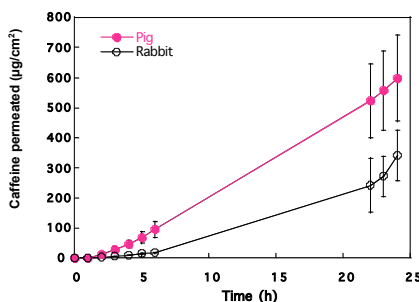
Stratum corneum lipid composition (% of total lipid content)

	Pig	Rabbit
Ceramides NS	20.7±2.5	24.5±0.9
Ceramides AS	22.7±2.6	10.2±0.9
FFA (oleic acid)	22.5±1.1	16.3±0.6
Cholesterol	31.5±0.3	11.4±0.8
Triglycerides (oleine)	1.1±0.1	5.1±2.4
Cholesterol esters (Cholesterol oleate)	1.5±0.2	32.5±11.4
Squalene	0	0

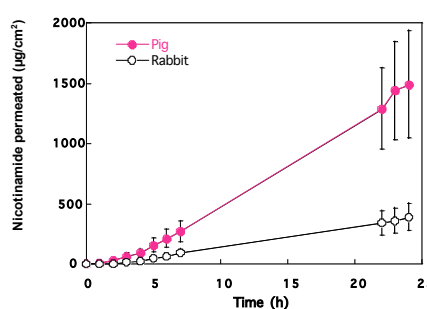
Despite the total amount of lipids extracted was similar in pig and rabbit SC (5 and 6% of the initial weight of SC for pig and rabbit respectively) notable differences exist in the composition of the two extracts. The overall results obtained indicate that rabbit SC is composed by a substantially higher percentage of nonpolar lipids, such as cholesterol esters and triglycerides, compared to pig skin.

Permeability

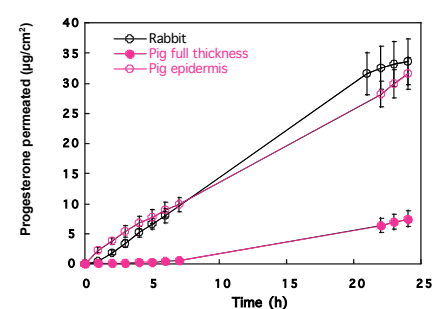
Caffeine



Nicotinamide



Progesterone



Conclusions

Overall the results obtained in this work support the usefulness of rabbit ear skin as barrier for skin penetration studies, for both lipophilic and hydrophilic permeants, even though its lipid composition is different from human skin.

References

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- 3) Lampe MA, Burlingame AL, Whitney J, Williams ML, Brown BE, Roitman E, Elias PM, J Lipid Res 1983;24:120-130.