

# CHARACTERIZATION OF HUMAN SCLERA IN VIEW OF TRANSSCLERAL IONTOPHORESIS:

M1217

## DETERMINATION OF THE ISOELECTRIC POINT

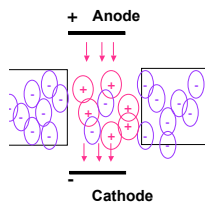
Sara Nicoli<sup>1</sup>, Marinella Quarta<sup>1</sup>, Giulio Ferrari<sup>2</sup>, Patrizia Santi<sup>1</sup>

<sup>1</sup>Department of Pharmacy, University of Parma, Italy<sup>2</sup> Department of Ophthalmology, University of Parma, Italy



### PURPOSE

Purpose of this work is to characterize human sclera in terms of permselectivity, in view of the application of transscleral iontophoresis. Iontophoresis is a technique that consists in the application of a low intensity current to enhance the permeation of drugs through a membrane. Transport mechanisms involved are electrorepulsion and electroosmosis.



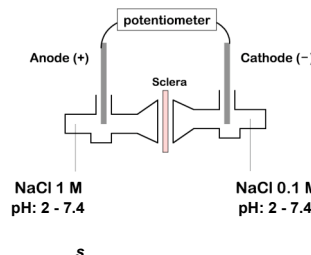
Electroosmosis is a convective solvent flow caused by the application of current to a charged membrane. It depends on the isoelectric point of the membrane, in this case the sclera.

The specific goal of this work is the determination of human sclera isoelectric point through the measurement of sodium transport number ( $t_{Na^+}$ ).

In order to find a model for human sclera, also porcine sclera was studied and compared to human sclera in term of thickness, water content, isoelectric point and passive permeability toward acetaminophen.

### EXPERIMENTAL SECTION

#### MEASUREMENT OF $Na^+$ TRANSPORT NUMBER



$$t_{Na^+} = 0.5 + \frac{FV_m}{2RT \ln \frac{C_2}{C_1}}$$

$V_m$  = membrane potential (V)  
 $R$  = Gas constant ( $J mol^{-1} K^{-1}$ )  
 $T$  = Absolute temperature (K)  
 $F$  = Faraday's constant (96478 C/mol)

- Excised human or pig sclera (frozen)
- Measurement of the potential (Multimeter)
- $V_m = V_{measured} - V_{electrode}$
- Calculation of  $t_{Na^+}$  (Luzardo-Alvarez A. et al 1998. Pharm Res 15:984-987)

#### PERMEATION EXPERIMENTS

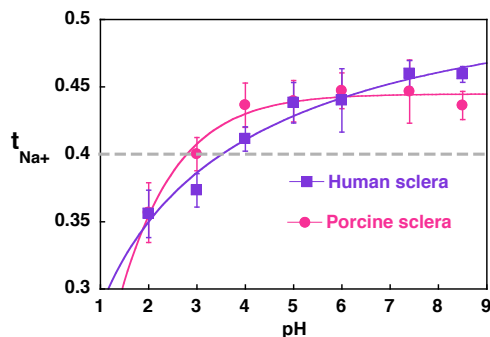
- Excised human or pig sclera (frozen)
- Permeation area: 0.6 cm<sup>2</sup>
- Donor: acetaminophen (MW 151), 33mM in HEPES buffer pH 7.4 added of NaCl 0.9%
- Receptor phase: HEPES buffer pH 7.4 added of NaCl 0.9%; T: 37°C
- Experiment time: 2 h
- HPLC-UV analysis

### RESULTS

#### CHARACTERISTICS OF HUMAN AND PIG SCLERA

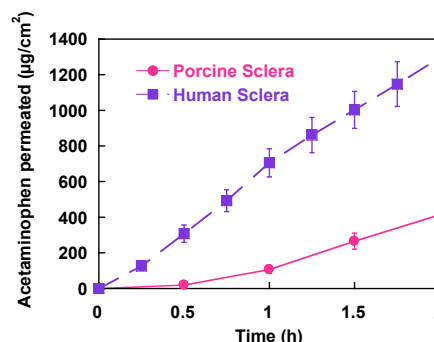
	Human	Porcine
Mean thickness (mm)	0.59±0.0 8	1.25±0.2 5
% H <sub>2</sub> O	71.6±0.6 3	69.5±1.1 8
Resistance (K ohm)	1.05	0.97±0.4 7

#### HUMAN AND PIG SCLERA ISOELECTRIC POINT

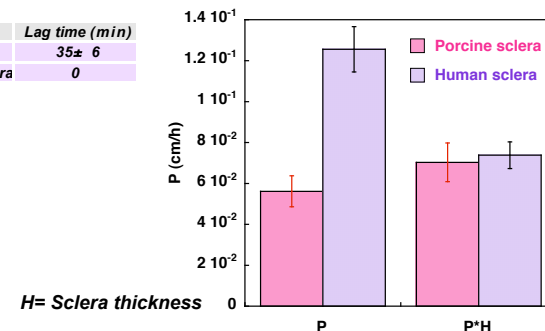


The isoelectric point of human and pig sclera is between 3 and 4 (where  $t_{Na^+}$  assume the value of 0.4)

#### ACETAMINOPHEN PERMEABILITY THROUGH PORCINE AND HUMAN SCLERA



	Lag time (min)
Pig Sclera	35± 6
Human Sclera	0



### CONCLUSION

- The isoelectric point of both human and pig sclera is included between 3 and 4
- Human and pig sclera are negatively charged at physiological pH
- Human sclera is significantly thinner than pig sclera
- Differences in acetaminophen permeability between human and pig sclera are due to different tissue thickness
- Pig sclera is a reasonable model for human sclera