

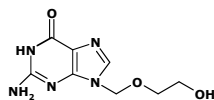
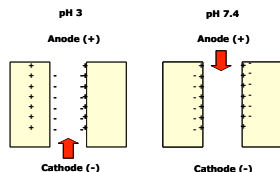
Effect of electroosmotic flow on permeation and skin accumulation of acyclovir during transdermal iontophoresis



F. Sartori, C. Padula, F. Marra, P. Colombo, P. Santi, Department of Pharmacy, University of Parma, Italy

INTRODUCTION

The skin is a permselective membrane with an isoelectric point of ~4. At pH 7 the skin supports a negative charge. When an electric field is imposed across the membrane, under normal condition, there is a net flow of solvent in the direction of counterion movement. As a result of this phenomenon, iontophoresis has been used to enhance the transdermal transport of not only ionic species, but also of neutral substances.



Acyclovir (ACV) is a synthetic analogue of 2'-deoxy-guanosine used in the treatment of cutaneous herpes virus infection. It is an ampholyte drug containing two ionizable groups with $pK_{a1}=2.4$ and $pK_{a2}=9.2$.

AIM OF THE WORK

The aim of this work was to evaluate the effect of electroosmotic solvent flow on the iontophoretic permeation of acyclovir (ACV) from a saturated solution at pH 5.8, where this molecule is unionized.

Objectives

To determine the amount of ACV permeated and accumulated in epidermis and dermis at different current densities, during anodal iontophoresis.

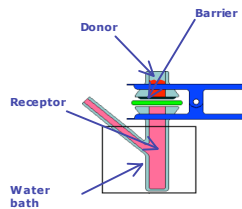
METHODOLOGY

Permeation experiments

- > Franz diffusion cells
- > Barrier: rabbit ear skin
- > Donor solution: ACV aqueous saturated solution pH 5.8 (1.2 mg/ml)
- > Receptor solution: PBS (pH 7.4)
- > Current density: 0.06, 0.125, 0.25, 0.5 mA/cm² (anodal iontophoresis)

ACV extraction

- > Heat separation dermis/epidermis
- > Extraction:
 - 0.5 ml distilled water
 - 60°C for 30 min
 - 0.5 ml HClO₄ 1N
 - 5000 rpm for 10 min

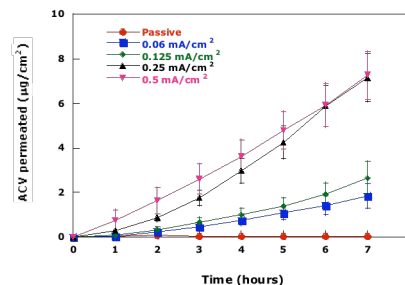


HPLC analysis

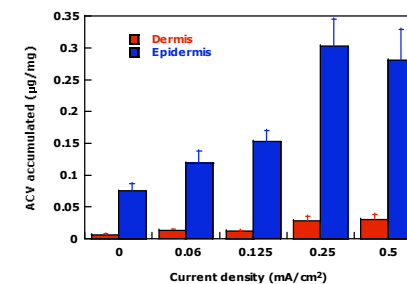
- > C₁₈ column from Vydac (Hesperia, CA, USA)
- > Mobile phase: water
- > Flux: 1.2 ml/min
- > UV detection at 254 nm

RESULTS

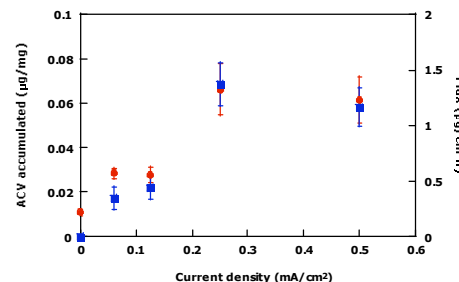
ACV permeation (anodal iontophoresis, pH 5.8)



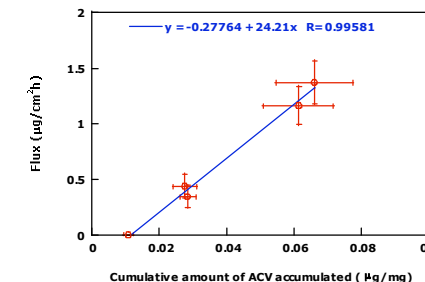
ACV skin accumulation (anodal iontophoresis, pH 5.8)



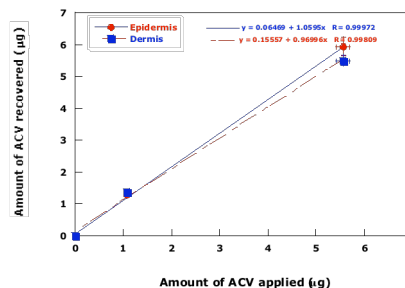
Effect of current density



Relationship between flux and amount accumulated



Recovery



CONCLUSIONS

- > The electroosmotic flow increased permeation and skin accumulation of unionised ACV.
- > ACV flux and skin accumulation increased with current density, although the relationship was not linear.
- > Flux and accumulation data were linearly related.