

ALPHA HYDROXYACIDS AND IONTOPHORESIS AS PENETRATION ENHANCERS

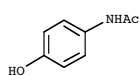
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AIM OF THE WORK

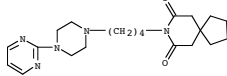
The purpose of this work was the evaluation of **lactic acid (1)** and **iontophoresis** as penetration enhancers for the transdermal permeation of different drugs with different physico-chemical characteristics:

ACETAMINOPHEN



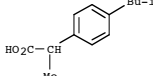
fw: 151.2

BUSPIRON



fw: 385.6
pKa: 7.2

IBUPROFEN



fw: 206.3
pKa: 4.45

METHODOLOGY

Permeation experiments:

Franz-type diffusion cells (0.6 cm²)

Rabbit ear skin

Donor compartment:

1 ml drug solution in HEPES buffer at pH 6 containing lactic acid (0%, 0.013%, 0.13%, 15% w/w)

Drug concentration: **ibuprofen 294 µg/ml**

acetaminophen 5 mg/ml

buspirone 10 mg/ml

iontophoresis:

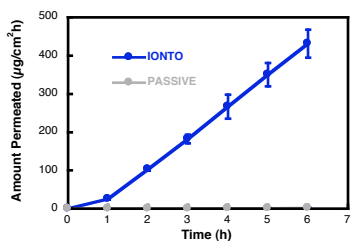
0.5 mA/cm²

anodal (buspirone, acetaminophen)

cathodal (ibuprofen)

RESULTS

IONTOPHORESIS (pH 6)

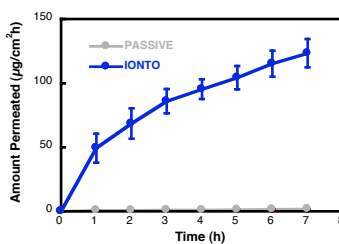


Buspirone (98.4% charged)

Anodal iontophoresis

Electrorepulsion

EF: 75

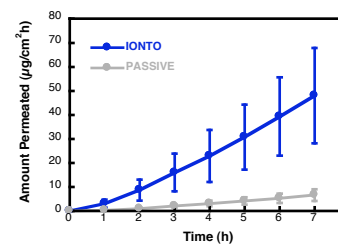


Ibuprofen (94.1% charged)

Cathodal iontophoresis

Electrorepulsion

EF: 66



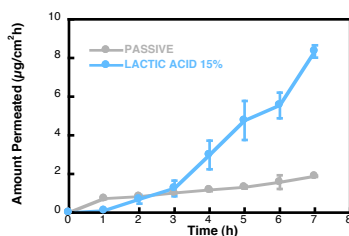
Acetaminophen (100% uncharged)

Anodal iontophoresis

Electrosmosis

EF: 7

LACTIC ACID (15%)



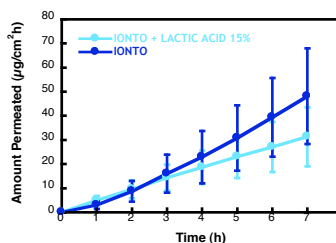
Ibuprofen: enhancement EF: 4

Buspirone: no enhancement

Acetaminophen: no enhancement

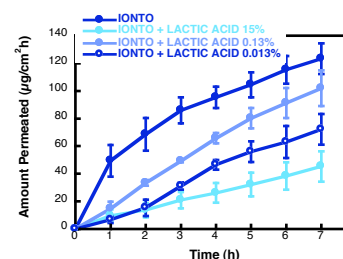
The enhancing effect of lactic acid on ibuprofen transport is probably due to its targeted action towards corneodesmosomes (corneodesmolytic).

IONTOPHORESIS + LACTIC ACID



Acetaminophen (100% uncharged)

Anodal iontophoresis

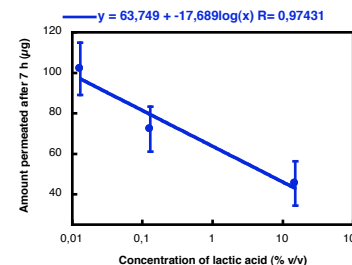


Ibuprofen (94.1% charged)

Cathodal iontophoresis

The amount of drug permeated decreased in comparison to iontophoresis alone, probably because of the competition of lactic acid for current transport (2).

A logarithmic relation was found between drug flux and lactic acid concentration.



CONCLUSIONS

- Iontophoresis is an efficient enhancing technique for drugs with different molecular weight and physico-chemical characteristics.
- Lactic acid behaves like a penetration enhancer only with **ibuprofen** (EF=4), while it is un-effective with the other molecules tested.
- The association of lactic acid and iontophoresis did not enhance the **acetaminophen** permeation with respect to iontophoresis alone.

- Due to the competition in current transport, the association of lactic acid and iontophoresis decreased **ibuprofen** transport: a logarithmic relation was found between drug flux and lactic acid concentration

REFERENCE

- (1) Harding CR, Watkinson A, Rawlings AV, Dry skin, moisturization and corneodesmolysis, Int J Cosm Sci (2000) 22: 21-52
- (2) Marro D, Kalia YN, Delgado-Charro MB, Guy RH, Optimizing iontophoretic drug delivery: identification and distribution of the charge-carrying species, Pharm Res. 2001 18(12):1709-13.