

# TRANSDERMAL DELIVERY OF RUTIN



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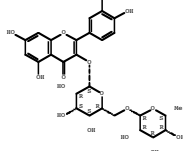
## AIM OF THE WORK

Rutin is a member of bioflavonoids. Bioflavonoids, due to their antioxidant properties (1), are known for their ability to strengthen and modulate the permeability of the walls of blood vessels including capillaries.

The transdermal administration of this molecule is very difficult, due to its low water-solubility and to its high molecular weight (664.58).

The aim of the work was to compound rutin in a vehicle able to enhance its permeation through the skin.

Chemical enhancers and iontophoresis (2) were evaluated.



## METHODOLOGY

1. **Rutin analysis:** HPLC method. Novapak® C18 column (Waters, Milford, MA, USA). The mobile phase was a mixture of methanol (36.7%), acetic acid (0.3%) and water (63%) at 0.8 ml/min. The UV detector was set at 261 nm.

2. **Solubility of rutin:** Rutin solubility was determined by adding an excess amount of drug to the vehicle. The dispersions were magnetically stirred at room temperature for 24 hours, filtered, and analysed.

3. **Permeation experiments:**

Franz-type diffusion cells (0.6 cm<sup>2</sup>).

Rabbit ear skin

Donor compartment : 1 ml of rutin saturated solution in different vehicles

Iontophoresis: anodal; 0.5 mA/cm<sup>2</sup>

## RESULTS

### SOLUBILITY

Vehicle	Rutin solubility (mg/ml)
Water	0.07 ± 0.01
Betacyclodextrin 0.01M	0.27 ± 0.07
Ethanol	5.82 ± 1.07
Ethanol + Lauric acid (4%)	12 ± 3
Ethanol: Water (50:50)	5 ± 1
PG	125 ± 8
PG + Lauric acid (4%)	138 ± 5
PG + Lauric acid (4%) + Menthol (2%)	75 ± 8

Rutin solubility in different vehicles.

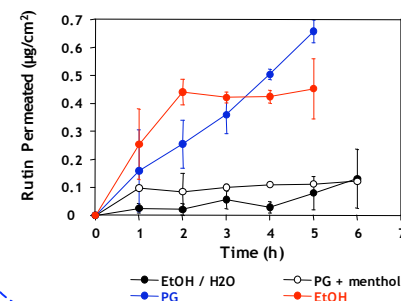
### TRANSDERMAL PERMEATION

Vehicles:

Water  
Betacyclodextrin 0.01M  
Propylenglycol (PG)  
Ethanol  
Ethanol/water 50:50

NO FLUX

Enhancer: lauric acid (4%)



### IONTOPHORESIS

Rutin is an uncharged molecule

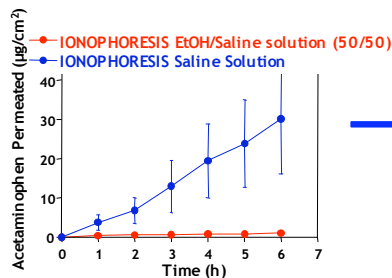
Enhancement mechanism: ELECTROSMOSIS

Anodal Iontophoresis pH 7.4  
Rutin saturated solution in Ethanol / Saline (50/50)

NO FLUX

Why iontophoresis did not enhance the penetration of rutin?

Electroosmosis marker: Acetaminophen



Ethanol hinders the electroosmotic flow:

	Flux
EtOH/Saline:	0.15 µg cm <sup>-2</sup> h <sup>-1</sup>
Saline:	4.8 µg cm <sup>-2</sup> h <sup>-1</sup>

## CONCLUSIONS

- Using water, betacyclodextrin 0.01M, propylenglycol (PG), ethanol and ethanol/water 50:50 as vehicles rutin did not cross the skin.
- Lauric acid (4%) both in PG and in the mixture Ethanol/water was able to generate a measurable flux through rabbit skin
- Anodal iontophoresis did not enhance the transdermal penetration of rutin in the mixture Ethanol/Saline 50/50
- The presence of ethanol in the donor solution hindered the electroosmotic flow.

### REFERENCE

(1) Chen, Y.T., Zheng, R.L., Jia, Z.J. and Ju, Y. Flavonoids as superoxide scavengers and antioxidants. Free Radic. Biol. Med. 1990, 9, pp. 19-21

(2) BW Barry. Vehicle effect: what is an enhancer? In Shah VP, Maibach HI, editors. Topical drug bioavailability, bioequivalence and penetration, Plenum Press, New York 1993, pp 333-349