Effect of Pluronics on Acyclovir Skin Permeation and Accumulation

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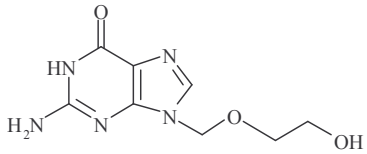
INTRODUCTION

Acyclovir (ACV) is one of the most effective agents against viruses of the Herpes group. The low efficacy of dermatological formulations of ACV was attributed to inadequate drug percutaneous penetration.

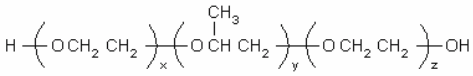
Pluronics® are low toxicity nonionic surfactants that could be used as penetration enhancer in order to achieve therapeutic local doses of low permeating drugs.



ACV

MW= 225.21

pK_{a1}= 2.4; pK_{a2}= 9.2



PLURONIC®

AIM

The aim of this work was to evaluate in vitro:

- the effect of different types and concentrations of Pluronic on ACV skin permeation and accumulation
- the effect obtained increasing ACV concentration in the drug solutions
- the effect of the time of contact of ACV solutions on skin permeation and accumulation.

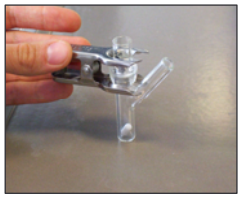
METHODS

Donor composition

Solutions pH 5.8	Pluronic (conc., % w/v)	ACV conc. (mg/ml)
Sol 1	-	1.0
Sol 2	F68 (5%)	2.6
Sol 3	F68 (5%)	1.1
Sol 4	F68 (10%)	1.3
Sol 5	F127 (5%)	1.6
Sol 6	L35 (5%)	1.5
Sol 7	L62 (5%)	1.4

Permeation test

- ✓ Rabbit ear frozen skin
- ✓ Vertical Franz type diffusion cells (area 0.6 cm^2)
- ✓ DONOR: 1 ml of ACV solutions (HEPES buffer pH 5.8)
- ✓ RECEPTOR: PBS (4 ml)
- ✓ Experimental conditions: 5 or 24 hs, 37°C



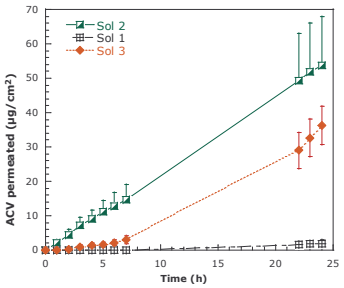
ACV skin extraction

✓Heat skin separation (epidermis/dermis)
✓0.5 ml of H_2O @60°C, 30' → 0.5 ml of $HClO_4$ → HPLC samples analysis

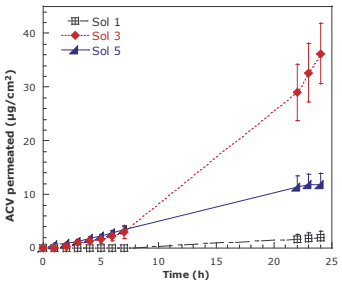
RESULTS

➢ **ACV permeation across rabbit ear skin (mean±s.e.m.):**

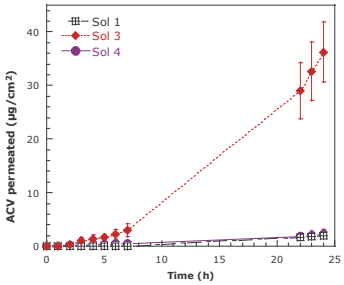
Effect of ACV concentration



Effect of different Pluronic®



Effect of Pluronic® F68 concentration



➢ **ACV skin accumulation (mean±s.e.m.):**

ACV solutions	Time of contact (h)			
	24		5	
	Epidermis (µg/mg)	Dermis (µg/mg)	Epidermis (µg/mg)	Dermis (µg/mg)
Sol 1	0.47±0.04	0.03±0.00	0.18±0.03	0.00±0.00
Sol 2	1.70±0.33	0.06±0.01	-	-
Sol 3	0.27±0.06	0.06±0.01	0.09±0.03	0.00±0.00
Sol 4	0.26±0.06	0.03±0.02	-	-
Sol 5	0.23±0.04	0.02±0.01	0.13±0.04	0.02±0.01
Sol 6	0.13±0.03	0.01±0.00	-	-
Sol 7	0.32±0.12	0.02±0.00	-	-

CONCLUSIONS

- ✓ Pluronic® F68 and, to a lower extent, F127 were able to influence ACV permeation across and accumulation into rabbit ear skin model
- ✓ The higher ACV concentration in donor solutions the higher was ACV flux and accumulation in skin
- ✓ Higher concentration of Pluronic® F68 did not affect ACV transport through the skin, compared to control solution
- ✓ In general, increasing the time of contact of ACV solutions with the skin, the amount of drug recovered increased.

ACKNOWLEDGMENTS:
Basf for Pluronic
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REFERENCES:

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