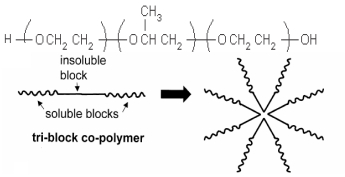
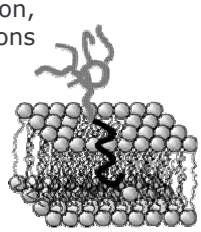
SIMULTANEOUS APPLICATION OF IONTOPHORESIS AND POLYMERIC MICELLES

Fabio Marra, Benedetta Vietti, Patrizia Santi
Department of Pharmacy, University of Parma, Parma, Italy

INTRODUCTION

Poloxamers are poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) block copolymers (PEO-PPO-PPO) forming micelles in aqueous solutions. Their characteristic depend on the block copolymer composition, the concentration and experimental conditions (temperature and presence of cosolutes).





OBJECTIVES

We intended to use Poloxamer micelles as transdermal drug carrier. Our attention was focused on Poloxamer 188 and Poloxamer 407. We characterized Poloxamer solutions by Dynamic Light Scattering (DLS) for size distribution. We investigated the effect of Poloxamer self-assembling properties on lidocaine penetration across and accumulation in the skin during transdermal iontophoresis.

METHODOLOGY

Donor solutions

Solution	Pluronic® F68	Pluronic® F127	Lidocaine
Control	—	—	1%
F127		5%	1%
F68	5%	—	1%

Pluronic solutions characterization

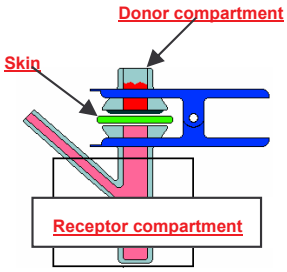
DLS of Pluronic® solutions at 25°C and 32°C (Zeta Plus, Brookhaven Instrument Corp., USA)

Permeation experiments

Experiments conducted for 24 hours at 37°C using:

- Franz type diffusion cells
- Donor: 1 ml of solution (HEPES Buffer pH 7.4)
- Membrane: frozen rabbit ear skin
- Receptor: 4.0 ml of saline solution (0.9% NaCl)
- Current: anodal at 0.5 mA/cm² for 5 hours

✓ At the end of the experiments the skin was separated in epidermis and dermis and lidocaine retained extracted.



✓ Samples analyzed by HPLC

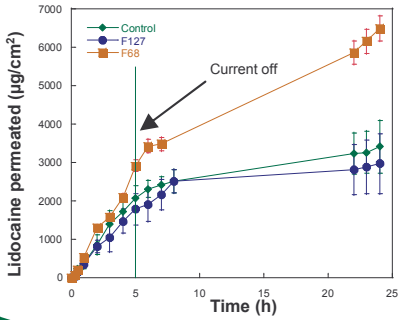
RESULTS

Pluronic®F127 solution characterization

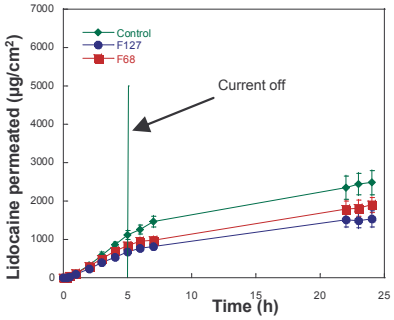
Solution (25 mM HEPES buffer pH 7.4)	Size at 25°C (nm)	PI at 25°C	Size at 32°C (nm)	PI at 32°C
NaCl 133 mM	26.0±0.3	0.152±0.016	21.4±0.3	0.082±0.027
Lidocaine 1% w/v	25.6±0.6	0.226±0.004	19.9±0.1	0.177±0.004
NaCl 133 mM, Lidocaine 1% w/v	24.6±0.2	0.212±0.009	19.3±0.1	0.166±0.005

Only Pluronic® F127 was able to form detectable micelles in our experimental conditions. Temperature increasing reduces micelles size and PI (polydispersity index).

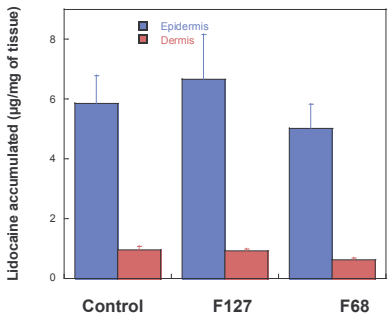
Iontophoresis without NaCl



Iontophoresis with NaCl



Lidocaine skin accumulation



CONCLUSIONS

✓ Pluronic® F127 was able to self assemble in nanometric micelles: micelles size was influenced by experimental conditions.

✓ The presence of competing ions reduces lidocaine skin permeation during transdermal iontophoresis

✓ Pluronic® F68 has a synergic effect during lidocaine transdermal iontophoresis without NaCl

✓ Pluronic® F127 reduces lidocaine permeation, but it slightly increases epidermal accumulation, if compared to Control and F68.

ACKNOWLEDGEMENTS

The authors greatly acknowledge BASF for supplying Pluronic® and Lisapharma S.p.A. (Erba, Como, I) for lidocaine.