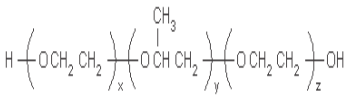
EFFECT OF POLOXAMER MICELLES ON IN VITRO LIDOCAINE SKIN PERMEATION AND ACCUMULATION

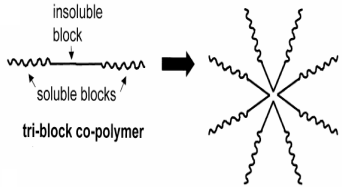
Fabio Marra, Benedetta Vietti, Cristina Padula, Sara Nicoli, Patrizia Santi
Department of Pharmacy, University of Parma, Italy

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).

Poloxamer





AIM

We explored the possibility to use Poloxamer micelles as suitable transdermal drug carrier. Our attention was focused on Poloxamer 188 and Poloxamer 407. We charaterized Poloxamer solutions using: Dynamic Light Scattering (DLS) for size distribution and Differential Scanning Calorimetry (DSC) for critical micellization temperature (cmt) determination. We investigated the effect of Poloxamer self-assembling properties on lidocaine penetration across and accumulation in the skin.

METHODS

Poloxamer solution composition (w/w, pH 7.4 buffer)

Solution	Poloxamer 188	Poloxamer 407	NaCl	Lidocaine
control	–	–	0,9	1%
Sol 1	5%	–	–	–
Sol 2	5%	–	0.9%	–
Sol 3	5%	–	–	1%
Sol 4	5%	–	0.9%	1%
Sol 5	–	5%	–	–
Sol 6	–	5%	0.9%	–
Sol 7	–	5%	–	1%
Sol 8	–	5%	0,9%	1%

Size distribution analysis: DLS

Measures performed by a Brookhaven Zeta Plus System at 25°C and 32°C.

Permeation experiments

Experiments conducted for 24 hs at 37°C using:
- Hanson Research Microette Plus automatic sampling system
- Donor: 1 ml of solution
- Membrane: frozen rabbit ear skin
- Receptor: 3.8 ml of saline solution (0.9% NaCl)

Cmt determination: DSC

DSC measures performed by a Mettler Toledo Star^e system:
- Temperature range: 0-70°C
- Scanning rate: 5°C/min.
- Cmt: onset of the peak.

At the end of the experiments the skin was separated in epidermis and dermis and lidocaine retained extracted by a validated method.

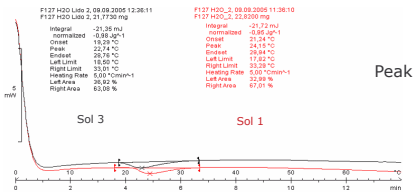
HPLC analysis

RESULTS

DLS and DSC analysis (mean±s.e.m.)

Solution (pH 7.4 buffer)	Size at 25°C (nm)	Polydispersity at 25°C	Size at 32°C (nm)	Cmt (mean±sd, °C)	Polydispersity at 32°C
Sol 5	28.0±0.5	0.213±0.003	19.0±0.2	21.18±0.04	0.148±0.004
Sol 6	26.0±0.3	0.152±0.016	21.4±0.3	20.70±0.10	0.082±0.027
Sol 7	25.6±0.6	0.226±0.004	19.9±0.1	19.30±0.47	0.177±0.004
Sol 8	24.6±0.2	0.212±0.009	19.3±0.1	18.20±0.40	0.166±0.005

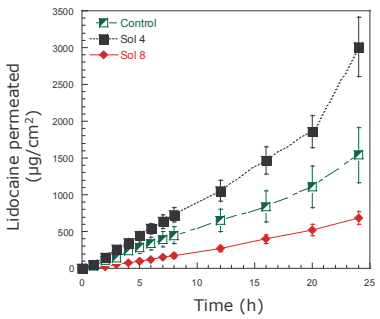
A typical endothermic peak due to micellization

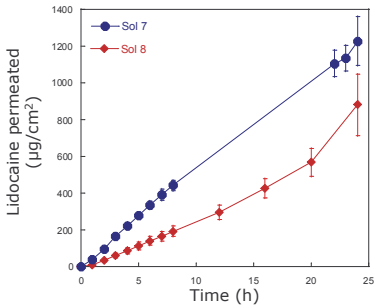


Peak onset= cmt

➢ Only **Poloxamer 407 at 5%** exhibited the ability to self-assemble.

Lidocaine permeation (mean±s.e.m.)





Skin retention of Lidocaine (mean±s.e.m.)

Solution	Lidocaine recovery (µg/mg)	
	Epidermis	Dermis
Control	4.61±0.64	0.63±0.13
Sol 4	3.67±0.70	0.83±0.17
Sol 7	5.07±0.58	0.58±0.05
Sol 8	5.94±1.06	0.68±0.12

CONCLUSIONS

- Poloxamer 407 at 5% was able to form nanosized micelles.
- The cmt was decreased by lidocaine, the presence of NaCl in solution and the increasing temperature.
- A 5% solution of Poloxamer 188 increased lidocaine permeation, while the release rate from Poloxamer 407 solutions decreased, if compaired to Control solution.
- The presence of NaCl, influencing micelles dimension, affects also lidocaine release. Permeation is higher from Poloxamer 407 5% without NaCl.
- No significant differences were noticed in lidocaine skin retention from the different solutions.

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