Investigation of the dynamics of water and lidocaine in a transdermal patch: QENS and in vitro permeation

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Introduction

Patch-non-Patch® is a non occlusive film intended for dermal and/or transdermal delivery. The peculiar characteristic of the film is that it is not adhesive in the dry state but it becames adhesive only when applied on the skin in the presence of small amount of water. Water plays an important role in terms of skin adhesion, and drug release from the transdermal film is related to the hydration of the polimeric components which is controlled by the amount of water used in its application.

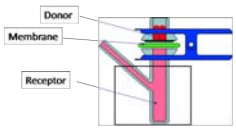
Aim of the work

To investigate the role and behavior of water molecules inside the monolayer bioadhesive film containing lidocaine, using the neutron scattering technique. Water and lidocaine mobility data obtained were compared with lidocaine permeation data obtained in vitro across silicone membranes.

Methodology

Permeation experiments

Membrane: silicone membrane (thickness 0.25 mm)
Receptor solution: NaCl 0.9%
Temperature: room temperature
Donor: containing lidocaine Patch-non-Patch® wetted with know amount of water (5, 15, 40, 55, 70 and 80%) and covered with a disc of polypropilene



Film composition

Component	% (w/w) on wet basis	% (w/w) on dry basis
Water	76.87	0.0
PVA 88K	11.20	36.0
Lidocaine HCl	8.00	25.7
Eudragit® E 100	4.29	13.8
Sorbitol	2.80	9.0
Lauric acid	2.48	8.0
Adipic acid	0.49	1.6
Glycerin	0.27	0.9

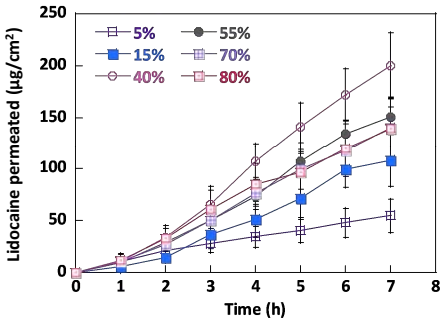
QENS experiments

- High resolution time-of-flight spectrometer IN5
- Incident wavelength 10 Å
- Average resolution 8μeV
- Room temperature
- Vanadium and pure water for standard correction

Results

In vitro permeation experiments across silicone membrane

Permeation profiles of lidocaine in the presence of different amounts of water

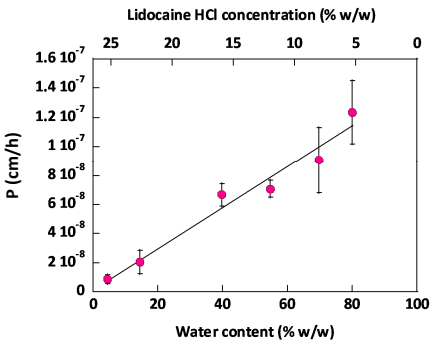


Hydration dependence of lidocaine flux

% of water	Lidocaine Flux (μg cm⁻² h⁻¹)	Lidocaine hydrochloride concentration (%)	Lidocaine Diffusion Coefficient (cm² s⁻¹) x 10⁷
5	6.71±2.33	25.33	n.d.
15	16.71±5.31	22.67	1.36±0.62
40	30.67±5.27	15.99	1.31±0.39*
55	26.25±2.19	11.97	1.23±0.53*
70	22.51±5.65	8.00	1.73±0.93
80	20.52±3.58	5.33	2.21±1.09

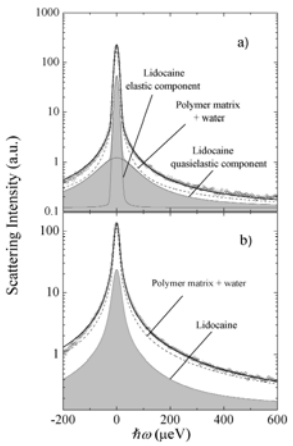
*=p<0.1 compared with the value obtained with 80% water content.

Hydration dependence of permeability coefficient of lidocaine

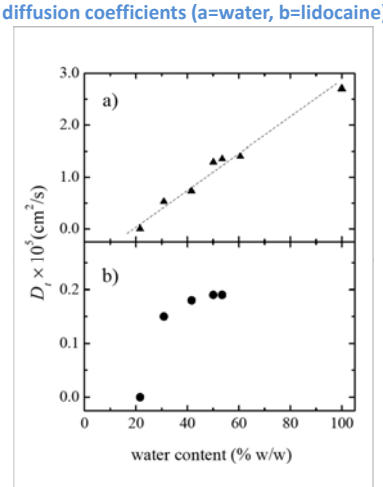


Quasi Elastic Neutron Scattering experiments

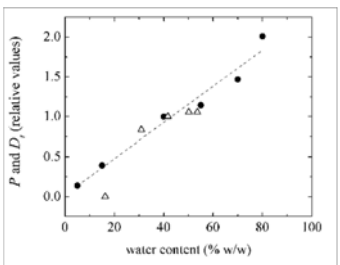
Quasielastic spectra at *Q*=1.02 Å of patches containing lidocaine at two different hydration levels (a=17%, b=49%)



Hydration dependence of the translational diffusion coefficients (a=water, b=lidocaine)



Hydration dependence of the lidocaine microscopic diffusion coefficients (Δ) and of the macroscopic permeability coefficient (●)



Conclusions

Both macroscopic and microscopic measurements indicate that film hydration plays a key role on the performance and efficiency of the Patch-non-Patch® system.

The diffusion of lidocaine depends on the presence of "mobile water".

Lidocaine permeation across silicone membrane data confirm this results because the presence of water produces an increase of lidocaine permeability coefficient.

Acknowledgments

The authors acknowledge Lisapharma S.p.A. (Erba, Italy)

Chiara Chiapponi thanks CNR-INFM for the financial support provided by a PhD grant.