Gordon Research Conference

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The 11th Barrier Function of Mammalian Barrier Function of Mammalian Skin Molecular, Biophysical & Biomechanical Understanding of Skin Barrier Formation, Function & Disease

August 9-14, 2009
Waterville Valley Resort
Waterville Valley, NH

Chairs:
Walter M. Holleran & Neil Kitson
Vice Chairs:
Gopinathan K. Menon & Juergen Lademann

The 11th Barrier Function of Mammalian Skin Gordon Research Conference is scheduled for August 9-14, 2009 at the Waterville Valley Resort in New Hampshire, USA. This conference represents the primary international research forum on the mammalian barrier, and is focused on the biophysical, biological, and clinical aspects of both normal and diseased barrier formation and function. The organizers have assembled an excellent program, with an outstanding list of speakers and discussion leaders to address the diverse aspects of current barrier research. To further insure that recent novel perspectives are highlighted, a "Hot Topics/Young Investigators" session is again scheduled, wherein six-to-seven presentations will be given by young scientists on their most-recent research.

This popular conference is generally fully- to over-subscribed, which makes it possible to accept an optimal mix of attendees from academics, industry and government, as well as a mix of young and established scientists. Submitted abstracts will be used not only to assist with consideration for conference participation, but also for the selection of presenters for the "Hot Topics/Young Investigators" session. The organizers also are making a concerted effort to recruit speakers and encourage attendees from around the world, particularly from Asia, Eastern Europe, and Former Soviet Union countries.

The 2009 Barrier Gordon Conference promises to provide new insights into the origin, function, maintenance, and repair of the mammalian skin barrier, including the penetration of drugs and exclusion of toxins and pathogens. The resulting exchange will hopefully lead to immediate, practical consequences for patients with skin and other disorders. To accomplish this goal, an array of important topics has been selected, with individual sessions and/or selected presentations devoted to: Molecular regulation and matrix signaling in barrier formation and regeneration; Insights into barrier structure and function from IR, deuterium NMR, & CARS spectroscopy; Membrane lipid transport and ABC transporter proteins in lamellar body formation and skin barrier function; Skin biophysics and biomechanics; Skin as a psycho-sensory barrier organ; Other barriers/other worlds: lessons from lung, GI, and bile barriers; Clinical dimensions of defective barriers in skin disease and repair; Anti-microbial and innate barriers; Protease regulation in stratum corneum structure, function, and disease; and Barrier electrophysiology. To complement these diverse themes, three evening poster sessions are scheduled, with up to 30 presentations each to be organized by topic. The always-entertaining Thursday evening debate returns with the topic: Math vs. Mouse: Percutaneous penetration & modeling.

Contributors

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Unilever
Wyeth Pharmaceuticals

SUNDAY

2:00 pm - 9:00 pm	Arrival and Check-in (Office Closed 6:00 pm - 7:00 pm)
6:00 pm	Dinner
7:30 pm - 7:40 pm	Welcome / Introductory Comments by GRC Site Staff & Conference Chairs
7:40 pm - 9:30 pm	**MEMBRANE BIOPHYSICS & SKIN BIOMECHANICS**
	Discussion Leaders: **Jenifer Thewalt** (Simon Fraser University, Vancouver, Canada) and **Juergen Lademan** (Charite Hospital, Berlin, Germany)
7:40 pm - 8:05 pm	**Evan Evans** (University of British Columbia, Vancouver) "Membrane biophysics and the skin"
8:05 pm - 8:20 pm	Discussion
8:20 pm - 8:45 pm	**Michel Lafleur** (University of Montreal, Quebec) "Organization and phase behavior of stratum corneum lipids"
8:45 pm - 9:00 pm	Discussion

9:00 pm - 9:20 pm	**Jamshed Anwar** (University of Bradford, UK) "Simulations of skin barrier function "
9:20 pm - 9:30 pm	Discussion
MONDAY	
7:30 am - 8:30 am	Breakfast
9:00 am - 12:30 pm	**BARRIER STRUCTURE AND FUNCTION: INSIGHTS FROM NOVEL TECHNOLOGIES & APPLICATIONS**
	Discussion Leaders: **Reinhard Neubert** (Martin Luther University, Halle, Germany) and **Jerry Kasting** (University of Cincinnati College of Pharmacy)
9:00 am - 9:25 am	**Luis A. Bagatolli** (University of Southern Denmark, Odense, Denmark) "Visualization of lipid domains in skin structure and transdermal delivery of liposomes"
9:25 am - 9:40 am	Discussion
9:40 am - 10:05 am	**Sunney Xie** (Harvard University, Cambridge, MA) "Skin imaging with Coherent Raman Spectroscopy (CARS)"
10:05 am - 10:20 am	Discussion
10:20 am	Coffee Break / Group Photo
10:40 am - 11:05 am	**Annett Schroeter** (Martin Luther University, Halle, Germany) "Role of ceramide [AP] for the structural assembly of stratum corneum lipids"
11:05 am - 11:20 am	Discussion
11:20 am - 11:45 am	**Joke Bouwstra** (Center for Biopharm. Sciences, Leiden University, The Netherlands) "Novel insights in the skin barrier lipid organization"
11:45 am - 12:00 pm	Discussion
12:00 pm - 12:10 pm	**Guy German** (Yale University, New Haven, CT) "Imaging stress in the stratum corneum during dehydration"
12:10 pm - 12:15 pm	Discussion
12:15 pm - 12:25 pm	**Jeroen van Smeden** (Leiden University, The Netherlands) "Development of a quick & robust detection method for skin ceramides"
12:25 pm - 12:30 pm	Discussion
12:30 pm	Lunch
1:30 pm - 4:00 pm	Free Time
4:00 pm - 6:00 pm	Poster Session #1

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PHASE BEHAVIOR MODIFICATION OF STRATUM CORNEUM LIPIDS INDUCED BY BICELLES

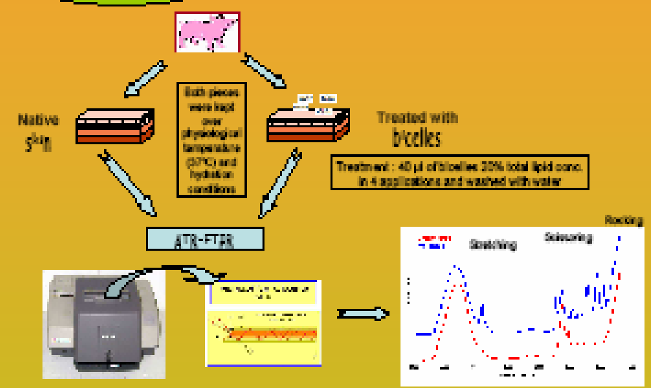
[1]G. Rodríguez, [1]L. Barbosa-Barros, [1]L. Rubio, A. Díez, [2]J. Estelrich, [1]A. De la Maza & [1]O. López
[1] I.Q.A.C.-C.S.I.C., Barcelona, Spain. [2] Facultad de Farmacia, UB, Barcelona, Spain

INTRODUCTION

Bicelles are lipid nanostructures formed by long and short chain phospholipids dispersed in aqueous solution normally used as membrane models[1]. Depending on different variables these structures may display a bilayered discoidal morphology with dimensions around 10-20nm diameter and 4-5 nm thickness that would be suitable for skin penetration. The aim of the present work was to evaluate the effect of bicellar systems in the stratum corneum (SC) of the skin *in vitro*.

Objective:
To evaluate the conformational changes in Stratum Corneum lipids by effect of bicellar systems.

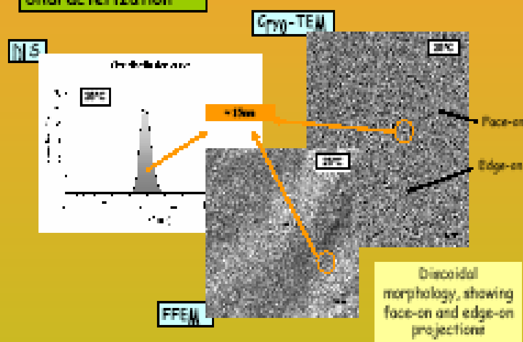
EXPERIMENTAL



RESULTS

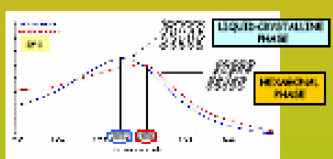
DMPC/DHPC bicelles q=2

Characterization



Discoidal morphology, showing face-on and edge-on projections

Stretching

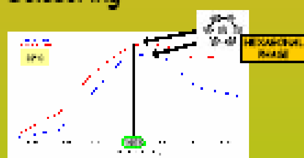


Temperature (ºC)	Stretching band (cm^{-1})	
	Native sample	Treated Sample
32	2850.2	2852.5
37	2851.6	2852.8
45	2852.0	2853.0

CH_2 stretching vibration provides information about chain conformation of the lipids[2,3]. Before treatment (native sample) the characteristic vibration of hexagonal phase (2850 cm^{-1}) is observed. When the bicelles are applied the vibration is shifted to higher value (2852cm^{-1}) that correspond with liquid-crystalline phase.

When temperature increase (see table) the band of native sample shift to higher values indicating an order-disorder transition from HEX to LIQ phases (from 2850.2 to 2852 cm^{-1}). However, after bicelles treatment a band around 2852 cm^{-1}, compatible with a LIQ packing lattice, is shown at all the temperatures.

Scissoring



Temperature (ºC)	Scissoring band (cm^{-1})	
	Native sample	Treated Sample
32	1467.8	1467.5
37	1467.9 1463.4-1471.7	1467.4
45	1467.8 1471.8	1467.2

CH_2 scissoring mode provides information about the lateral packing of the lipids in the SC[2,3]. At 32ºC for both samples (before and after treatment) only one peak is observed. This peak is around 1468cm^{-1} that correspond with hexagonal phase.
When temperature increases (see table) for native sample the same peak that 32ºC is observed for all temperatures. At 37º C the split (1464 and 1472 cm^{-1}) characteristic of orthorhombic phase was noted. At 45ºC one of the peaks of the split was lost. After treatment with bicelles only a peak at 1467 cm^{-1} is observed that clearly indicates a hexagonal packing lattice for all the temperatures.

CONCLUSION

- Before treatment, stretching and scissoring vibrations indicate an unique gel phase in the SC.
- After treatment with bicelles, stretching vibration shows a conformational change in the alkyl chain of lipids, from gel to liquid crystalline phase. Lateral packing keeps in gel phase indicating a coexistence of phases (gel and liquid crystalline)
- Bicelles induce certain disorganization of the SC lipids by formation of fluid domains. This fact could be related with a modification of the skin barrier function.

REFERENCES
[1] Triba, M. N., D. E. Warschawski, and P. F. Devaux. 2005. Reinvestigation by Phosphorus NMR of Lipid Distribution in Bicelles. *Biophys. J.* 88: 1887–1901
[2] Boncheva, M.; Damien, F.; Normand, V. 2008. Molecular organization of the lipid matrix in intact stratum corneum using ATR-FTIR spectroscopy. *Biochim. Biophys. Acta.* 1778: 1344-1355.
[3] Gooris, G.S.; Bouwstra, J.A. 2007. Infrared spectroscopic study of stratum corneum model membranes prepared from human ceramides, cholesterol, and fatty acids. *Biophys. J.* 92: 2785-2795

galen.rodriguez@iqab.csic.es