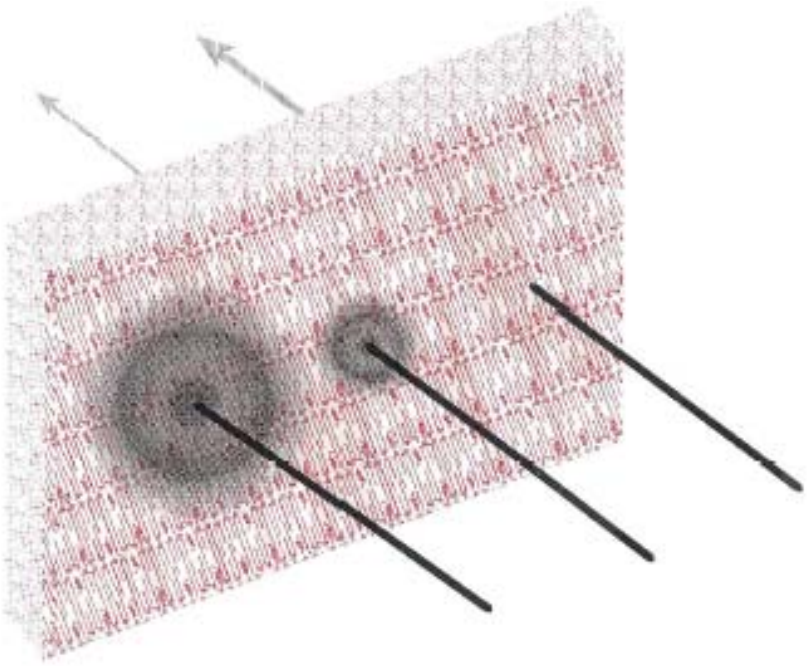
Perspectives in Percutaneous Penetration

Volume 10a



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BICELLAR SYSTEMS FOR SKIN TREATMENT

O LÓPEZ[1], LB BARROS[1], C BARBA[1], M CÓCERA[2], C LÓPEZ-IGLESIAS[3], L CODERCH[1] and A DE LA MAZA[1]

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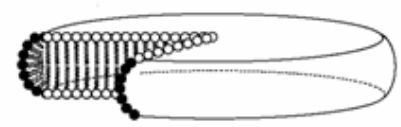
Bicelles are discoidal aggregates constituted by a flat dimyristoyl-glycero-phosphocholine (DMPC) bilayer, stabilized by a rim of dihexanoyl-glycero-phosphocholine (DHPC) in water (fig. 1). Nowadays, the use of these systems is mainly based on their ability to be aligned in magnetic fields. Thus, the bicelles are used to orient membrane proteins that can be inserted in the bilayer structure and also to study the superficial interactions between proteins and the phospholipid bilayer[1].

Figure 1: Bicellar structure



The bilayered structure and dimensions of bicelles, with diameters in the range of 10-50 nm and thickness about 6 nm, are similar to those of liposomes and micelles. These two nanostructures are often used for skin treatment, although their application is in debate due to some aspects[2]. Liposomes seem to be too large to penetrate into the narrow interlamellar spaces of stratum corneum (SC) lipids. Concerning the micelles, the usual presence of surfactant in their composition supposes a problem due to the well known irritative effect of these solubilizing agents on the skin. In this line, the use of bicelles for skin treatment could reports advantages on the use of liposomes and micelles: the size of bicelles is small enough for passing through the SC lipid lamellae and their composition consists completely on lipids. Thus, the objective of our work is to evaluate the use of these structures, the bicelles, for topical application.

Two different biceIlar systems, DMPC/DHPC and DMPC/DHPC/ceramides, were formed by a method based on cycles of heating(40ºC)-sonication-cooling(0ºC)-sonication[3]. Characterization of these systems was performed by freeze-fracture electron microscopy (FFEM) and by dynamic light scattering (DLS)[3]. The ability of these nanostructures to improve the barrier function was evaluated “in vivo” by topical application of bicelles on the forearm of human volunteers. Biophysical properties of the skin, such as hydration, elasticity and skin capacitance, were measured in healthy and in SDS disturbed skin. To study the effect of the bicellar systems on the microstructure of the SC “in vitro”, pieces of tissue, native and disturbed, were treated separately and under the same conditions with the aforementioned bicellar systems. The evaluation of the SC samples microstructure was carried out by freeze-substitution applied to transmission electron microscopy (FSEM).

Our results demonstrated that depending on the lipid composition, bicellar systems presented a variety of shapes and sizes. “In vivo” experiments showed that bicelles are able to accelerate the repairing of skin conditions. The effect of systems containing ceramides was specially noted. Microscopy study of the interaction of the bicelles with SC “in vitro” showed alterations in the structure of this tissue. These alterations were related to the visualization of additional structures in the SC intercellular spaces and were clearly noted when disturbed SC was used instead of native SC. Given that the new structures detected are consequence of the treatment with bicelles, we assume that, at least, part of the lipids from the bicelles is retained in the SC. This supplement of lipids could induce changes in the phase behaviour of the SC lipid and could be the cause of the alterations on skin biophysical properties detected “in vivo”. Results of this work indicate that bicellar systems constitute a promising nanostructure for topical application able to reinforce skin conditions supplementing additional lipids to the SC. The possibility of using the bicelles as transdermal delivery systems should be considered in future works.

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2. O López et al (2002) Reconstruction of liposomes inside the intercellualr lipid domain of the stratum corneum, Langmuir, 18, 7002-7008
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