

Abstract

Charles University, Faculty of Pharmacy in Hradec Králové

Department of Pharmaceutical Technology

Author: Eliška Šrámová

Supervisor: Dr. Georgios Paraskevopoulos, Ph. D

Consultant: Mgr. Anna Nováčková

Title of Thesis: Study of the effect of cholesterol concentration on monolayer models

Skin is composed of 3 major layers: hypodermis, dermis, and epidermis. The uppermost layer, which is called *stratum corneum* (SC), has a unique structure resembling a well-built wall. Corneocytes represent bricks and the lipid matrix works like a mortar. Ceramides, free fatty acids, and cholesterol (Chol) are the main lipids creating the human SC matrix. In a healthy SC, the ratio of these lipids is equimolar. This ratio is crucial, not only to maintain the barrier function of the skin, but also for the organization of lipids in SC. Chol appears to be required for the correct lamellar organization, and the ordering of lipids inside of the lamellar formation (lateral organization) in SC. Abnormalities in the ratio of the lipids and depleted amount of Chol can lead to a disruption of the skin barrier function resulting in skin disease or multisystemic diseases (e.g. X-linked ichthyosis, Conradi-Hünemann-Happle syndrome, and CHILD syndrome.)

The present work deals with a Chol deficiency study on lipid organization on monolayer models simulating the lipid matrix. Langmuir monolayers at the gas-liquid interface, Brewster angle microscopy, and atomic force microscopy (AFM) were used as characterization techniques. The main characteristic of all recorded isotherms is their gradual shape (slow increase of surface pressure when mean molecular area is decreased). The steepest isotherm was observed for the sample where Chol was 80 % of its physiological concentration. The lipid organization was always depended on the composition of the samples. More specifically, the mean molecular area of single samples when surface pressure is 1.5 mN/m ($A_{1,5}$) was significantly different between each other. On the other hand, the A_{20} values showed only negligible variation. The elasticity of monolayers is increasing when the concentration of Chol is getting lower (until Chol is 40 % of its physiological concentration). For lower concentrations, an opposite dependence was noticed. A similar trend like elasticity was observed for the size of lipid domains by AFM where the smallest size was noticed at the 40 % Chol sample.