

Shiseido Successfully Develops Jointly with Keio University a Novel Lipid Substrate that Evaluates Stratum Corneum Intercellular Lipids

Elucidates Damage and Repair Processes of Stratum Corneum Intercellular Lipids

Shiseido Co., Ltd. (Head Office: Chuo-ku, Tokyo; hereinafter “Shiseido”) has successfully developed jointly with Keio Leading-edge Laboratory of Science and Technology (within the Faculty of Science and Technology, Keio University, Yokohama city, Kanagawa; hereinafter “KLL”) a novel lipid substrate that enables evaluation research at the laboratory level on the alignment structure of stratum corneum intercellular lipids (hereinafter “SCIL”), which play an important role for the stratum corneum, the outer-most layer of the skin. With this development, changes in the conformation and dynamics of lipids from when SCIL have received external damage until they are repaired—the detailed process of which has been unclear until now—has been elucidated for the first time.

In the future, Shiseido plans to actively promote the development of skincare products and usability evaluation using this lipid substrate.

Structure and Role of SCIL

The stratum corneum is made up of corneocytes and SCIL, which serve as a “mortar” to adhere between the layered corneocytes and thus perform a crucial function as a barrier that protects living cells in the body from the external environment (Figure 1).

SCIL are mainly comprised of ceramides, fatty acids and cholesterol. Among various barrier functions, SCIL are recognized as important tissues, which prevent moisture evaporation within the skin and the entry of foreign substances. Additionally, these lipids also have been recognized as forming an organized structure that is systematically aligned and that this structure and skin conditions are closely related.

Development of Novel Lipid Substrate for Conducting Research on SCIL Alignment Structure

In cases where the human stratum corneum was used for repeatedly carrying out detailed research on the alignment structure of SCIL, which are important tissues, issues were previously raised including the difficulties of conducting analysis since the stratum corneum is comprised of many types of lipids and corneocytes are present, and there is a low measurement reproducibility due to the variation among individuals.

In order to resolve these issues, measures were taken to develop a totally novel lipid substrate* as an alternative to human stratum corneum, thereby enabling repeatability of in-depth evaluation research at the laboratory level.

Three issues had to be addressed in the development of a new lipid substrate: 1) type of lipid to be used and composition, 2) detailed examination of preparation method, and 3) verification that the prepared lipid substrate has similar physicochemical properties as SCIL derived from the human stratum corneum.

Shiseido has embarked upon a joint research project with KLL since 2006 directed toward developing a novel lipid substrate (Project Leader: Former professor Haruma Kawaguchi of Keio University), in which joint research was promoted with former KLL professor Toyoko Imae, who is a pioneer in the development of the preparation method of lipid substrates, which requires advanced techniques related to biointerface chemistry.

The development of a novel lipid substrate was promoted with the objective of realizing a simple lipid composition and concise preparation method to allow this substrate to be broadly utilized in R&D on a daily basis. Based on this research principle and as a result of repeatedly examining various aspects, an original preparation method was discovered using a specific type of ceramide, fatty acid and cholesterol. This finding consequently contributed to the successful development of novel lipid substrate (Figure 2) that has similar thermal properties as human SCIL and a periodic lamellar structure.

Note: Previously developed lipid substrates were mainly for conducting research on percutaneous absorption of medical agents.

Elucidation of Damage and Repair Processes of SCIL Using Novel Lipid Substrate

Research was conducted using the novel lipid substrate in order to clarify the conditions and processes of SCIL, which perform a crucial function as a skin barrier, in cases where SCIL are affected by external damage at the molecular level. With regard to the impact of external damage, effects were examined when an aqueous solution of sodium dodecyl sulfate (SDS) generally used for rough skin tests came into contact with the lipid substrate. As a result of measurements by means of infrared absorption spectrum and X-ray diffraction, disarray of the aligned structure and structural change of ceramide molecules occurred in a short period of time when the SDS aqueous solution came into contact with the lipid substrate. Also, a phenomenon was observed, in which the cholesterol and fatty acid began to elute from the lipid substrate. Moreover, when most of the cholesterol and fatty acid eluted over a long period of time, it was discovered that the ceramide was almost the only lipid comprising the substrate.

At the same time, with regard to the repair of damaged SCIL, effects were examined using a similar measurement method as described above, whereby the cholesterol and fatty acid eluted over a short period of time were applied to the damaged lipid substrate, which had been pretreated with the SDS aqueous solution. As a result, the structure of the ceramide affected by the SDS aqueous solution was restored to its original structure in a short period of time when the cholesterol was applied (Figure 3). Furthermore, when the fatty acid was simultaneously applied, the damaged lipid substrate was restored to its original condition together with the penetration of these lipids. In other words, these results suggested that application of types of cholesterols is effective in repairing damaged SCIL.

The current achievements in developing a new lipid substrate was presented at the Symposium on Macromolecules held on September 16-18, 2009 in Kumamoto, Japan.

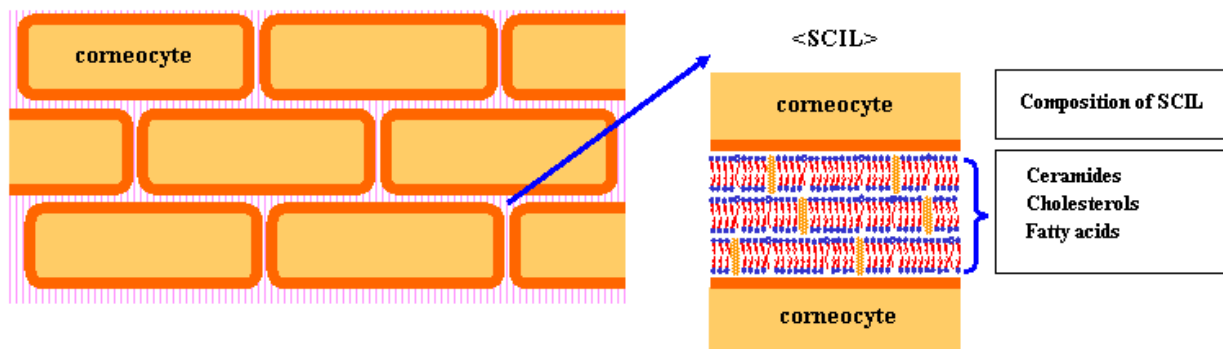


Figure 1 Schematic Model of Stratum Corneum



Figure 2 Novel Lipid Substrate

When repaired, peak originating from the ceramide shifts to direction indicated by the arrow.

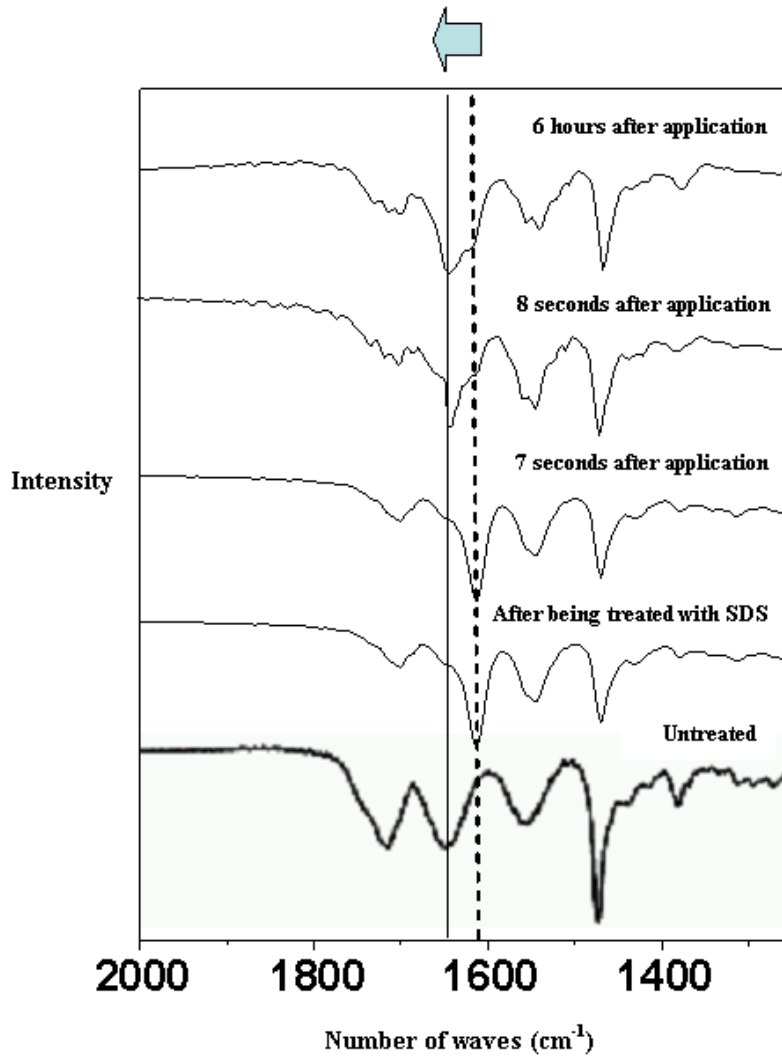


Figure 3 Repair Effects by Applying Cholesterol (Infrared Absorption Spectrometry)