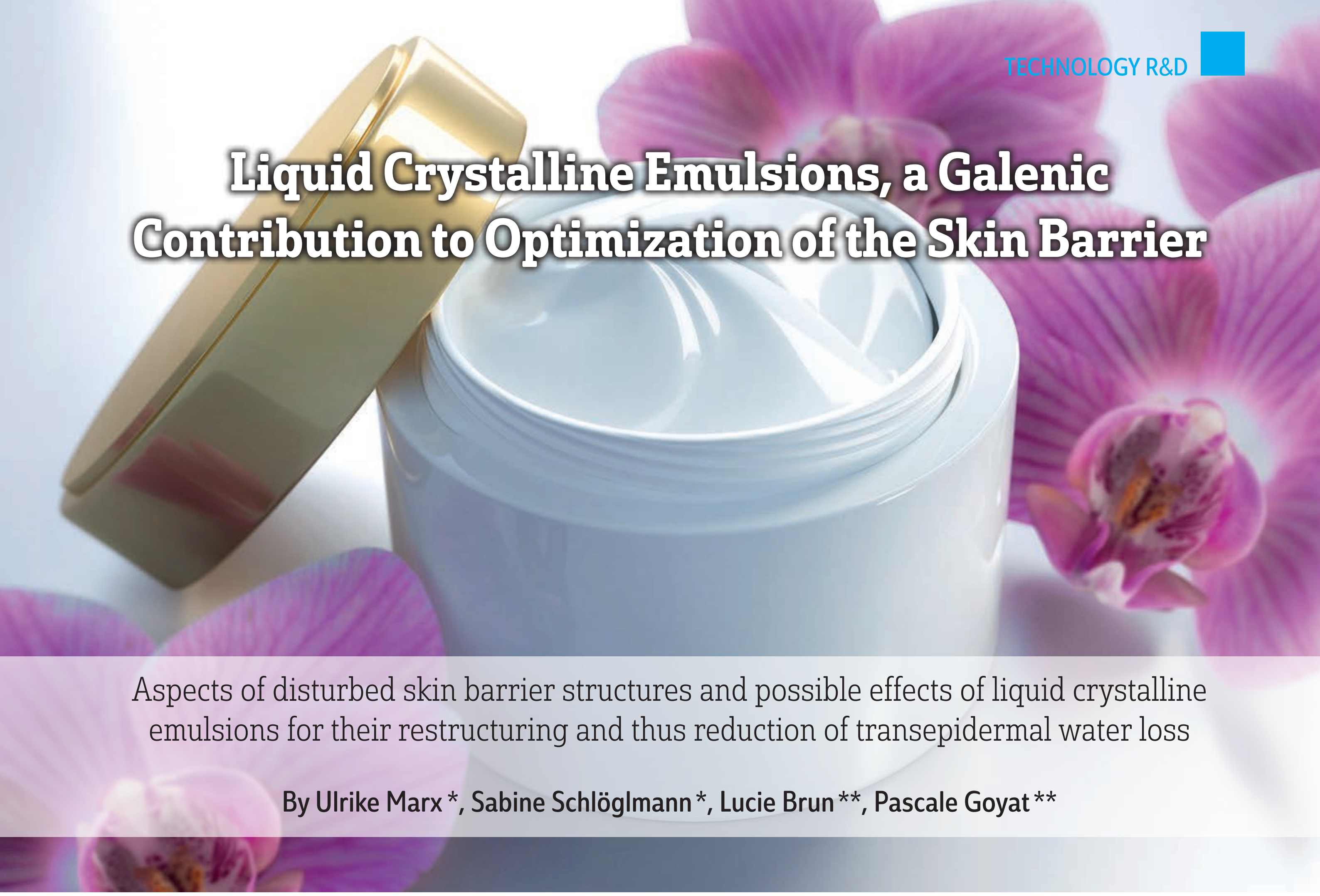

Liquid Crystalline Emulsions, a Galenic Contribution to Optimization of the Skin Barrier

Aspects of disturbed skin barrier structures and possible effects of liquid crystalline emulsions for their restructuring and thus reduction of transepidermal water loss

By Ulrike Marx *, Sabine Schlöglmann *, Lucie Brun **, Pascale Goyat **

Face and skin care today is based on results of scientific research dealing with optimal skin health. This is the basis for a radiant and young looking of the skin. Currently, highly-effective skin care products work with active ingredients which are available in a broad range. Another very important factor in promoting skin vitality is the preservation and, as far as possible, restructuring of the natural skin barrier function. This is emphasized again and again by dermatologists and appropriate formulations for skin care are required.[1, 2]

This article intends to show that a sophisticated structure of an emulsion essentially contributes to the improvement and optimization of skin structure and health.

Protective mechanisms of the skin via structured Stratum corneum lipids

The Stratum corneum of intact skin possesses protective barriers that regulate the transepidermal water loss (TEWL) and protect against the ingress of external pollutants.

The regulation of the TEWL ensures a high moisture content of the skin which, in addition to a cushioning effect, also ensures the optimum flow of biological processes in the skin, e.g. the functioning of the cells and their membranes, nutrient transport, reaction processes and the removal of metabolites from these biological skin processes.

Most of the substances that affect our skin from the environment are not able to penetrate an intact Stratum corneum, either because the molecules or particles are too large or because they are not capable of passing skin protection mechanisms such as the barrier membranes[1]. The intact barrier membranes consist of Stratum corneum lipids which form stretched bi-lamellar structures with arrange multi-lamellar and form alternating lipophilic/hydrophilic “barrier layers” (Figure 1).[1, 5]

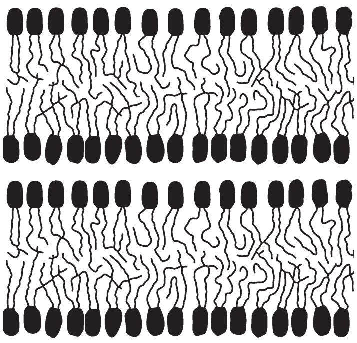

Fig. 1: Sketchy: Section of the structure of the barrier membranes

The bi-lamellar structures of the Stratum corneum are referred to as Landmann units and can be visualized by transmission elec-

* NCD Ingredients GMBH, Hanau, Deutschland;
** Natura-Tec, Fréjus, France

tron microscopy. They are in a highly organized, multi-lamellar form, which is similar in structure to the bi-lamellar envelope structure of liposomes (which, however, are present in globular form). Landmann units are found almost everywhere in the intercellular space of the stratum corneum of an intact skin (Fig. 2).[4] Most active ingredients that are to become active in the deeper layers of the skin, have structures that are similar to the skin's own structures or are liposomally encapsulated and therefore can mostly pass those.

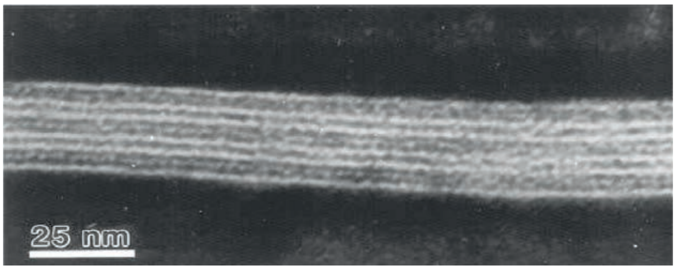

Fig. 2: Normal structure of the lipid lamellae in the intercellular space. Here are three Landmann units that separate the dark-colored corneocytes above and below this intercellular space.[4]

If the barrier is disturbed or no longer present, the skin loses an important part of its protective mechanism against water loss or penetration of harmful substances. It is believed that the Landmann units can be negativly influenced by strong amphiphilic substances such as surfactants and also partly emulsifiers with a very high HLB value (substances which have a very strong tendency to form globular structures).[3,4] The flat-stretched structures shift around and the Landmann units disappear.

It has been shown that the lamellar Landmann structures are largely intact in children's and young people's skin, but are usually only partially or rarely found in adults. The structured systems disappear and unstructured lipid agglomerates appear. Then part of the skin barrier is disturbed and a reasonably unhindered penetration of not too large molecules in both directions is significantly easier.[4]

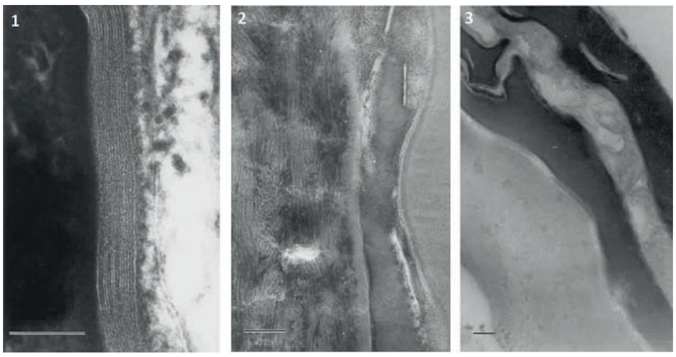

Fig. 3: (1) Landmann units from the outer SC of a person 24-years old (Landman units are present). (2) Mixture of amorphous materials with different textures in the intercellular space of the outer SC from a person 28 years old. (3) Lipid structure from a person 49 years old, intercellular spaces appear to contain largely amorphous material.[4]

Also medical factors such as age, skin disease and hormone status can influence the penetration processes.[12]

Under which conditions do multi-lamellar structures emerge?

The bi-lamellar stretched forms appear due to structuring of molecules with predominantly mild to moderate amphiphilia. Means, they are lipophilic molecular chains having one or more hydrophilic moieties as we know e.g. of emulsifiers. Important for a lamellar stretched arrangement is that the lipophilic part of the molecule takes up the same amount of space in this arrangement as the polar one. For the polar group, not only their size and shape but also the intensity of the polarity is crucial in terms of space requirements.[5, 13] Fig. 6 shows how these space requirements result in curvature of interfaces.

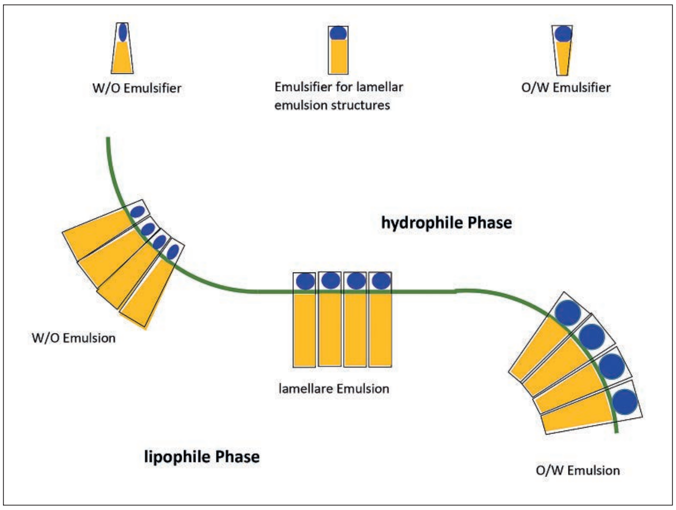

Fig. 4: Interface curvature due to space requirements of the lipophilic and hydrophilic moiety of an emulsifier.

In order to produce lamellar structures, one usually works with combinations of O/W emulsifiers with only low polar co-emulsifiers or lipids, in order to create a space requirement compensation.

The less polar co-emulsifiers and lipids are integrated into the structures but have a much smaller footprint in the polar area and a higher in the lipophilic area. As a result, they influence or straighten the degree of curvature and a stretched structure results (sketched in Fig. 5). Lamellar bilayers of such structures can then be arranged into multi-lamellar forms, as is the case with the intact skin barrier.

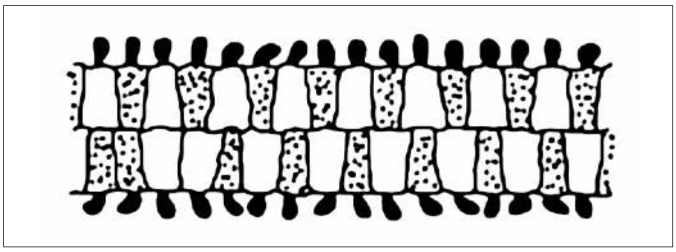

Fig. 5: Amphiphilic molecules with different space requirements in an interface structure together as a flat membrane unit.[5]

Low polar amphiphilic substances, co-emulsifiers or lipids, with corresponding properties, in simple structure are, e.g. Glycerol monostearate, fatty alcohols, possibly also fatty acids. In the range of the active substance-like lipids squalane / squalene, ceramides, cholesterol and other basically similar molecular structures are suitable. [5, 6, 7, 8, 9, 10, 18]

The addition of co-emulsifiers increases the total amount of emulsifier molecules available and approaches a lamellar emulsion form from an additional side, as these structures require a higher amount of such molecules. [5, 13]

Ingredient properties that influence the structuring in formulations

How should one ideally choose emulsifiers and lipid phases? There are some general things about the structure of the molecules and the composition of basic formulations that in most cases lead to the goal of a liquid crystalline structure in an emulsion.

The papers "Effect of Moisturizers on the Structure of Lipids in the Outer Stratum Corneum of Humans" [4] and "Study on the Formation and Properties of Liquid Crystal Emulsion in Cosmetic" [14] discuss, among other things, how specific emulsifiers, lipids, and humectants [11] affect the restructuring of the Landmann units and the TEWL. [3, 4, 5, 6, 15, 16]

In principle, the choice of emulsifier and co-emulsifier is the most important influencing factor. There are various emulsifier molecules and complexes with a known tendency to form liquid-crystalline systems, which thus lay the foundation for the formulation of liquid-crystalline structured emulsion formulations. These multi-lamellar structures, both stretched and globular, can be visualized using a microscope and polarized light (Fig. 6). [4, 8, 9, 14, 15]

Whether the formulations form globular or stretched lamellar structures is subject to the factors mentioned above. The question now arises whether it is essential to have a lamellar stretched, Landmann unit-like structure already in the emulsion or if it is possible to achieve the desired effects in the skin even by globular systems. This question has received an important impulse through the publication "Study on the Formation and Properties of Liquid Crystal Emulsion in Cosmetics" [14]. In this work it is shown that a liquid crystal emulsion with globular structure turns into a lamellar form in the first 10 minutes after application (Figure 6), which is mainly explained by the water evaporation on the skin and concomitant increase of concentration.

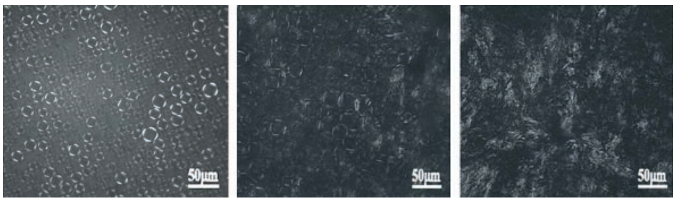

Fig. 6: Liquid crystalline structures under the microscope and polarized light: (1) liquid-crystalline emulsion in globular structure (so-called „Maltese crosses"), (2) the same emulsion directly after application (globular structures are still visible but already lamellar structures can be detected), (3) – same emulsion 10 min after application changed to lamellar structures

It is known that C16-18 fatty alcohols particularly promote the liquid-crystalline structures in emulsions [10]. The above study [14] also shows that increasing the content of C16-18 fatty alcohol and the resulting increased liquid-crystalline structure in the tested emulsion slows down transepidermal water loss (Fig. 7). The water content of the upper skin layer was not affected. Formulating with complementary further humectants and actives should intensify this effect.

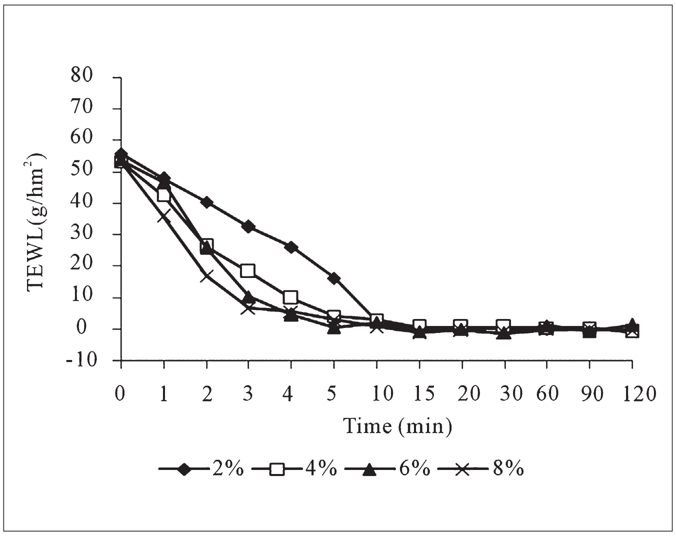

Fig. 7: Influence on TEWL: by C16-18 fatty alcohol lower and higher structured emulsions. [14]

Emulsifiers for liquid crystalline emulsions

As emulsifier molecules with a proven tendency to form liquid-crystalline systems, only a few examples, such as sucrose esters, (e.g. Sucrose Polystearate), acyl oligopeptides (e.g. Potassium Palmitoyl Hydrolyzed Wheat Protein), lecithins or acyl amino acids (e.g. Sodium Acyl Glutamate) should be mentioned here. For these corresponding information can be found in literature [i. a. 4, 9]. They are also particularly interesting since all can be used in the field of natural cosmetics.

Emulsifiers with a strong tendency to form liquid-crystalline emulsions are the emulsifier complexes **CRYSTAL CREAM** and **EMULACTIVE W** from Natura Tec/France. In both products, the main emulsifiers are selected from the molecular structures that are particularly known for the formation of liquid crystalline systems. Both emulsifier systems are Ecocert/Cosmos certified.

The main emulsifier used in **CRYSATL CREAM** is Sucrose Polystearate, the co-emulsifiers and lipids are Cetearyl Alcohol and the unsaponifiable fraction from Olive oil. Sucrose Polystearate is a sugar-based emulsifier known to have moisturizing properties and a pleasantly supple, non-oily skin feel. The super refined natural and renewable concentrate of Olive oil Unsaponifiables, brings in a high amount of Squalene, a skin friendly component and excellent biocompatible active. [4, 12,15,18] The combination with the rather dry effect of Cetearyl Alcohol, makes **CRYSTAL CREAM** an emulsifier which can be used to formulate emulsions of medium viscosity, very good absorption properties and a light yet grooming touch. In a test formulation with a short-chain triglyceride, as it is typically used in cosmetic emulsion formulations, **CRYSTAL CREAM** proves the formation of liquid-crystalline structures in globular form.

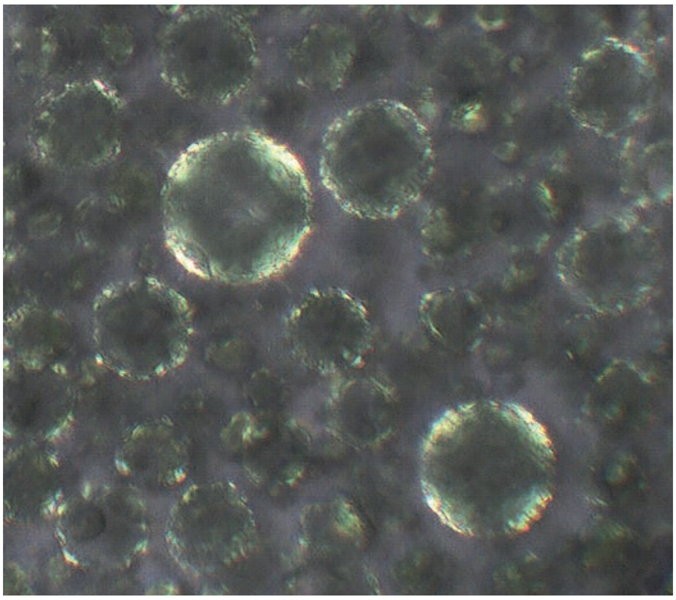

Fig. 8: Test formulation: Natura-Tec CRYSTAL CREAM 5%, Caprilic / Capric Triglyceride 20%, ad 100% water, preservative. Liquid-crystalline structures under the microscope and polarized light (X40).

EMULACTIVE W combines Potassium Palmitoyl Hydrolyzed Wheat Protein with Cetearyl Alcohol and Glyceryl Stearate. Due to the fact that the main emulsifier in this system has absolutely no oily feel **EMULACTIVE W** can be used to formulate particularly light, velvety and low to medium viscous liquid crystalline emulsions with correspondingly good spreadability. A gentle body is supplied by Glyceryl Stearate. In addition, the Potassium Palmitoyl Hydrolyzed Wheat Protein used here as an emulsifier is known from other applications as an active ingredient or molecule with particularly good skin-friendly properties.[4, 5, 7]

In addition to the possibilities of formulating emulsions with liquid-crystalline structures, **CRYSTAL CREAM** and **EMULACTIVE W** offer broad application possibilities that go beyond the range of directly generated liquid-crystalline phases.

The formulation of liquid-crystalline emulsion formulations is no longer a real challenge with the formulating know-how and emulsifiers available today. The advantages of such emulsion forms for the skin and its barrier function are proven. Therefore, the demand of dermatologists to follow this path, and to take advantage of such emulsion forms is understandable and feasible.

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