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Phospholipids for Cosmetic Products

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Phospholipids: Natural Functional Ingredients and Actives for Cosmetic Products

Introduction

In cosmetic products phospholipids are popular as biodegradable natural ingredients. The phospholipid molecule comprises a glycerol backbone which is esterified in positions 1 and 2 with fatty acids and in position 3 with phosphate. The systematic designation of e.g. phosphatidic acid (PA) is 1,2-diacyl-sn-glycero-3-phosphate (where sn means stereospecific numbering). The specific and non-random distribution of substituents over the positions 1,2 and 3 of the glycerol molecule introduces chirality. In typical membrane phospholipids, the phosphate group is further esterified with an additional alcohol, for instance in phosphatidylcholine (PC) with choline **(Fig. 1)**, in phosphatidylethanolamine (PE) with ethanolamine and in phosphatidylglycerol (PG) with glycerol. Depending upon the structure of the polar region and pH of the medium, PE and PC are zwitterionic and have a neutral charge at pH values of about 7, whereas e.g. PG is negatively charged.

Due to the molecular structure which is comprised of a hydrophilic part and a lipophilic part, phospholipids have a special amphiphilic character. When mixed with water, they form various structures depending on the number of fatty acids esterified to the glycerol backbone and the resulting geometry of the molecule. When only one fatty acid is esterified (monoacyl phospholipids/lysophospholipids) to the glycerol backbone, the molecules are cone shaped and they are able to form micelles. Di-acylphospholipids with cylindrical shape are organized as lipid bilayers (lamellarphase) with the

Abstract

Phospholipids can be used in cosmetic products in several ways. As a technical ingredient, phospholipids can be used as an emulsifier, a liposome former, a solubilizer and a wetting agent. On top of that, phospholipids are cosmetic actives. In this paper the characteristics for the use of soybean phosphatidylcholine (SPC) and hydrogenated soybean phosphatidylcholine (HSPC) in cosmetic products are compared. As cosmetic actives, natural phospholipids isolated from soy beans provide the essential fatty acids linoleic acid and linolenic acid. These phospholipids are renowned for their ability to maintain the skin in healthy condition and to ameliorate skin disorders like acne vulgaris and neurodermitis, or slow down skin aging. Furthermore they play a role to liquefy the stratum corneum and as penetration enhancer (SPC) or act as compounds which strengthen the skin barrier function (HSPC).The availability of multifunctional natural phospholipids in various grades and modifications with controlled quality provide the formulator a valuable tool box for designing optimal cosmetic products.

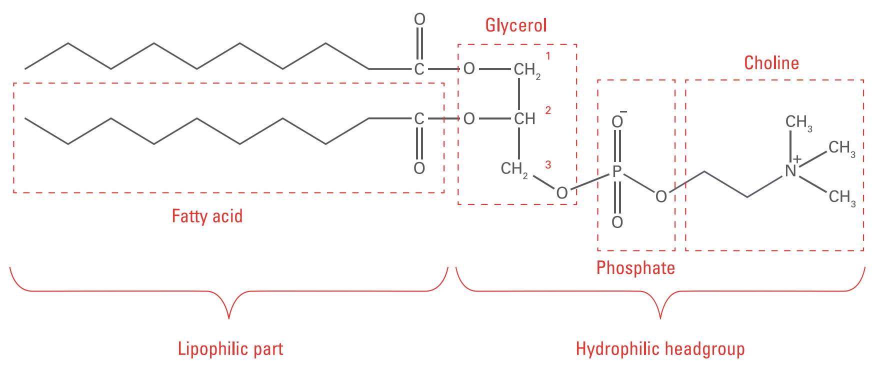

Fig. 1 Molecular structure of phosphatidylcholine

hydrophobic tails lined up against one another and the hydrophilic head-group facing the water on both sides **(Fig. 2)**. The latter structures formed are called liposomes. The membrane of such a liposome resembles the basic structures of cellular membranes. It is therefore obvious that such structures will have a beneficial interaction with skin cells.

In cosmetic formulations di-acylphosphatidylcholines are the main phospholipids used. In the literature lecithin is sometimes used as a synonym for phosphatidylcholine; the EU directive 2006/257/EC and CAS define lecithin as a phospholipid mixture containing besides mainly phosphatidylcholine other phospholipids and components such as fatty acids, triglycerides, sterols, carbohydrates and glycolipids. These lecithins can be fractionated with respect to their phosphatidylcholine content. In this way several grades can be produced starting from crude lecithin with ca. 15% PC still containing substantial amounts of the plant oil from which it has been isolated, and de-oiled or fractionated lecithin to obtain contents from 25-96% PC. Phospholipids are essential natural components of the membrane of all living cells; they are non-toxic and possess very high skin tolerability. For cosmetic use mainly phospholipids isolated from natural vegetable sources like soy beans, rapeseed (canola seed) and sunflower seed are used.

The isolated phospholipids have a fatty acid composition typical for the plant source used. The fatty acid composition of soybean phosphatidylcholine (SPC) is provided in **Table 1**.

Typical for these soybean phospholipids is the high total content of the omega-3 18:3 linolenic acid and omega-6 18:2 linoleic acid, which are essential fatty acids, and oleic acid. The fatty acid composition of phospholipids determines the temperature at which the fatty acids change their mobility. Below this so-called 'gel state to liquid crystalline state phase transition temperature' the fatty acids are rigid (gel state), whereas above this temperature the fatty acids are mobile (liquid crystalline or fluid state). Phospholipids containing polyunsaturated fatty acids have very low (below 0 °C) transition temperatures. This means that these lipids at skin temperatures of around 22°C are in the liquid crystalline state and form, upon hydration, very flexible structures/liposomes. Phospholipids containing unsaturated fatty acids can be converted to phospholipids with saturated fatty acids by means of hydrogenation. The resulting phospholipids are in the gel state at skin temperature and tend to form more rigid and stable membrane structures.

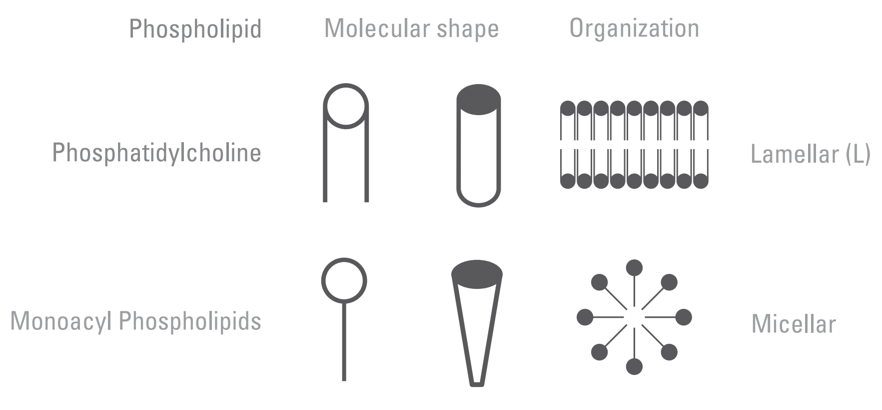

Fig. 2 Shape of phospholipid molecules dependent on polar head group and fatty acid composition and resulting aggregate organization upon hydration

Phospholipids: Multifunctional Cosmetic Ingredients and Actives

Because of their chemical structure and physicochemical properties, the use of phospholipids in cosmetic formulations has several unique aspects. In the following, it will be apparent that phospholipids are not only technically useful ingredients but support the barrier function of the skin as well. Hence Phospholipids will keep the skin in healthy condition and can therefore be considered as cosmetic actives. These functional properties of phospholipids are the basis for the excellent skin tolerability of phospholipids (2,3).

Technical ingredients

Di-acylphospholipids are very mild detergents (4,5). After hydration di-acylphospholipids with cylindrical shape do not form micelles like strong detergents but lamellar structures. For these reasons they are not able to emulsify oil with water spontaneously. However, when applying high pressure homogenization to make oil-in-water emulsions, they are excellent emulsifiers yielding very stable emulsions. Without oils, di-acylphospholipids form liposomes/lamellar structures similar to the skin spontaneously, simply by hydrating the phospholipids. The formed lamellar structures (liposomes) or emulsified oils are able to incorporate lipophilic compounds in formulations. Liposomes further allow the (simultane-

Fatty acid	In 1-position (%)	In 2-position (%)	Total (%)
C16:0 palmitic acid	24.0	1.7	12.9
C18:0 stearic acid	7.9	1.0	4.4
C18:1 oleic acid	10.9	10.0	10.5
C18:2 linoleic acid	52.4	80.6	66.5
C18:3 linolenic acid	4.7	6.7	5.7

Table 1 Fatty acid composition (mole %) of SPC determined by enzymatic hydrolysis followed by gas-chromatography (1)

ous) encapsulation of water soluble cosmetic components in their aqueous core. Phospholipids can also be used as wetting agents to disperse water insoluble compounds in aqueous vehicles.

Cosmetic actives

Upon application to the skin, unsaturated di-acylphospholipids like SPC act as a source of linoleic- and linolenic acid **(Table 1)**. The fraction of administered phospholipids containing linoleic acid reaching metabolic active skin cells may also strengthen the natural barrier function of the skin through incorporation into skin ceramides I. In addition, these phospholipids may play a role in the suppression of acne (6, 9), neurodermitis and psoriasis (10,11). The linolenic acid bound to phosphatidylcholine can be eventually converted to the omega-3 fatty acids docosahexaenoic acid (DHA, 22:6n-3) and eicosapentaenoic acid (EPA, 20:5n-3).

Dependent on their fatty acid composition, di-acylphosphatidylcholines, have a different interaction with the skin. In the following, this is described for (unsaturated) SPC and (saturated) hydrogenated soybean phosphatidylcholine (HSPC) (5)(12).

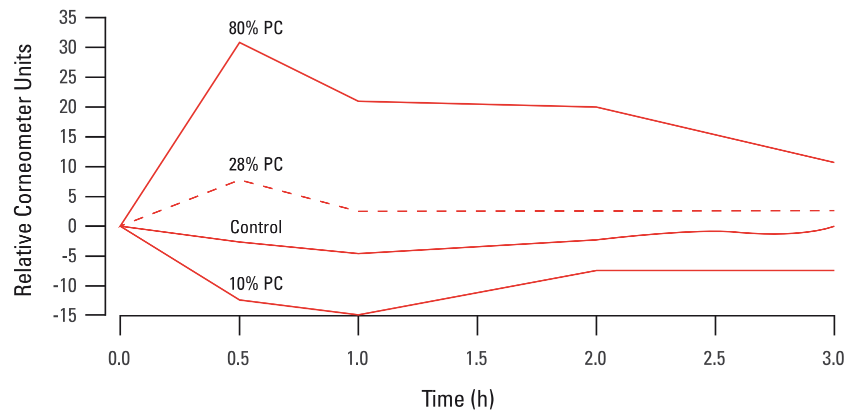

Fig. 3 Influence of SPC concentration in topical formulations on the humidity of the human skin after single application to ten healthy volunteers

Soybean phosphatidylcholine (SPC)

The influence of the SPC concentration on skin humidity was tested after single skin application of formulations containing 0% (control), 10%, 28% and 80% PC to ten volunteers.

The results obtained **(Fig. 3)** demonstrate an acute and significant increase in skin humidity for the formulation with 80% PC. The formulation with 28% exhibited a weaker effect, whereas the formulation with 10% PC showed a reduction in skin humidity. Since the only difference between these formulations is the PC content, it can be concluded that PC provides a moisturizing effect to the stratum corneum. This conclusion was confirmed by a second multiple application study, which showed an increase of skin humidity to steady state levels.

The influence of SPC on the skin roughness was studied by comparing an aqueous SPC liposome dispersion comprising of 20.6% w/v SPC (with 93% PC) and ca. 16% ethanol with an oil-in-water emulsion after multiple applications to 20 volunteers **(Fig. 4)**. The skin roughness was significantly decreased in the group treated with the SPC containing formulation.

In order to assess the degree of skin penetration of SPC liposomes, 3H labeled (in fatty acid) liposomes were applied to porcine skin non-occlusively at 1 mg phospholipid/cm^2 skin. After 30, 60 and 180 min the phospholipid concentration in the stratum corneum and underlying skin layers was determined using liquid scintillation counting on samples obtained by 20-fold stripping and subsequent tissue sampling (13, 14). The results provided in **Table 2**, show that more than 99% of the applied PC accumulates in the stratum corneum, suggesting that the liposomes strongly interact with the stratum corneum lipids. It is assumed that the ceramides, which are the main components of stratum corneum lipids, are diluted after a treatment with SPC liposomes, with the PC molecules by means

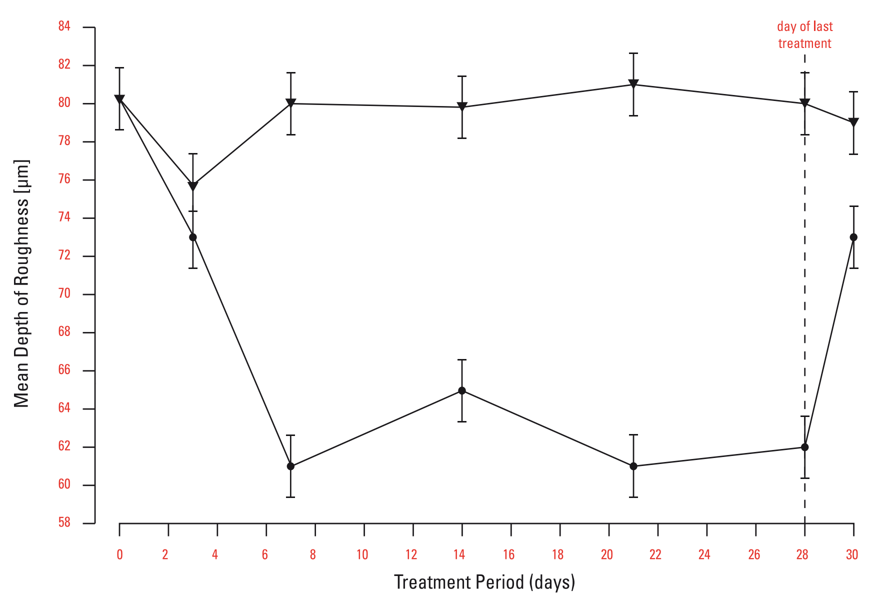

Fig. 4 Effect of a 20.6 % SPC-containing formulation on the roughness of the human skin after multiple application to healthy volunteers (n=20). •-• SPC containing formulation; ▼-▼ o/w emulsion

of a fusion process of the liposomes with the membranes of the stratum corneum. The fluidity of the lipid barrier is thereby increased. The depth of modification is strongly dependent on the concentration of PC.
An SPC based product for cosmetic use from Lipoid Kosmetik AG is Natipide® II. It consists of densely packed multilamellar liposomes with a mean particle size in the range of 200-250 nm (15, 16).

Hydrogenated soy bean phosphatidylcholine (HSPC) (16)

In contrast to the fluid-state SPC, HSPC contains mainly saturated fatty acids at amounts of approximately 85% stearic acid, 14% palmitic acid, and 1% other fatty acids. These fatty acids have a high melting point and induce a high transition temperature of approximately 55 °C. At skin temperatures, hydrated dispersions of the lipids are therefore in the gel state and rigid in nature.

Comparison SPC and HSPC (14)

The different kinetics of the interaction between the native skin lipids and the fluid-state PC and/or HSPC were determined by several in vivo and in vitro penetration studies. Fluorescent labeled liposomes made from fluid-state PC penetrate significantly deeper into the rat skin than those composed of HSPC (18). The penetration of liposomes with encapsulated fluorescent dye carboxyfluorescein into the human abdomen skin studied by fluorescence microscopy showed that liposomes made from fluid-state PC compared to liposomes composed of HSPC are taken up by the skin more readily, permeate faster, and penetrate beyond the stratum corneum (19). These findings suggest that HSPC, and most probably also the accompanying water, is taken up by the stratum corneum but not by the deeper layers of the skin. In addition, HSPC does not seem to perturb the lipid barrier.
Topical formulations comprising of HSPC possess a skin protective function. They restore and stabilize the skin barrier layers. Measurement of the TEWL (transepidermal water loss) showed that formulations with HSPC do not influence the natural TEWL level. Formulations with HSPC comprise lamellar structures, which are layered on top of each other very similar to the skin structures (20).
A product which contains high concentrations of HSPC is Skin Lipid Matrix (SLM) from Lipoid Kosmetik AG **.
SPC, i.e. phosphatidylcholines with unsaturated fatty acids, form flexible liposomes which are able to penetrate more deeply into the skin compared to rigid liposomes/lamellar phases comprising of HSPC which for these reasons reside predominantly in the upper layers of the skin. SPCs are therefore more suitable as penetration enhancers / transportation vehicles enhancers to carry co-encapsulated compounds more deeply into the skin whereas formulations comprising of HSPC are more suitable to stabilize the barrier function of the skin.
Relevant parameters for the design of cosmetic formulations using both classes of phosphatidylcholines are provided in **Table 3** (21).

Skin Strips/Cuts	Skin Section	µg Liposomal Phospholipid/g Tissue
20 strips	Stratum corneum	100 000
1 mm	Epidermis	500
2 mm	Dermis	20
3 mm	Subcutis	8
4 mm	Subcutaneous fat	8
5 mm	Subcutaneous fat	12

Table 2 Penetration of ^{3}H labeled liposomes into porcine skin after three hours after single application at 1 mg phospholipid/cm^2 skin

Conclusions

Phospholipids are unique compounds for formulators of cosmetic products. This is owed to their multifunctional properties as a technical ingredient and cosmetic active in combination with their high degree of tolerability. The availability of these natural compounds with controlled quality in various grades and modifications provide the formulator with a valuable tool box for designing optimal cosmetic formulations.

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Parameter	SPC	HSPC
Fatty acid composition	Unsaturated fatty acids; linoleic, linolenic and oleic acid	Saturated fatty acids; stearic and palmitic acid
Phase transition temperature (°C)	Below 0	50-60
Structures upon hydration	Liposomes and lamellar structures dependent on process conditions	Liposomes and lamellar structures dependent on process conditions
Technical Ingredient		
Emulsifier Dispersing and solubilizing ability	Yes Hydrophilic, amphiphilic and lipophilic compounds	Yes Hydrophilic, amphiphilic and lipophilic compounds
Cosmetic Active		
Skin barrier function	Penetration enhancement; conditioning the SC* Penetrates into layers below SC	Stabilizing the barrier function; conditioning the SC Penetrates only into SC and not below
Barrier compatibility	Yes, slightly enhancing TEWL**	Yes, stabilizing normal TEWL
Supply of linoleic and linolenic acid	Yes; beneficial effects of phospholipids containing omega-3 and omega-6 fatty acids on acne vulgaris, psoriasis, neurodermitis	No
Tolerability	Very high: CIR*** report	Very high: CIR report

* SC: Stratum corneum, ** TEWL: Transepidermal water loss, *** CIR: Cosmetic Ingredient Review

Table 3 Relevant characteristics of SPC and HSPC for cosmetic products

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