

Cosmeceuticals – phospholipids

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When it comes to cosmeceuticals, often the classics prove to be the highly efficient products and not the new substances freshly out of the retort. Besides vitamins and essential fatty acids, also the phospholipids rank among the classics.

What are the particular features of phospholipids? In a nutshell: they have multifunctional effects, they are physiological, produced naturally in the body, biodegradable and they are free of adverse effects. Beyond that, they are components of our daily nutrition or contained in food supplements. In spite of their relatively high molecular mass, they are readily absorbed by the skin. Their history dates back to the beginnings of life on our planet.

Biomembranes

With the evolution of biomembranes from phospholipids, the first microorganisms could organize in cells and seal themselves off from the outside world. As the communication with the outside world and the transport of nutrients had to be ensured, the cellular biomembranes had developed a selective permeability that has been continually optimized in the course of time with the help of proteins integrated for this purpose. This particular set-up has not been changed until today. Hence phospholipids are ubiquitous where there are living cells, not only in microorganisms but also in all herbal and animal forms of life. Phospholipid extraction is a rather complicated process and the base materials used today are egg yolk and soya lecithin (majority). Soya lecithin more or less is a waste product in the soya oil production.

Compositions

Phospholipids consist of a glycerin, fatty acids and phosphoric acid containing backbone which is chemically bound to variable amino- or poly alcohols as e.g. choline, ethanolamine, glycerin, inositol, and serine.¹ The most important phospholipids occurring in mammalian membranes are:²

- phosphatidylcholine (PC; membrane fraction: 45-55%)
- phosphatidylethanolamine (PE; membrane fraction: 15 -25%)
- phosphatidylinositol (PI; membrane fraction: 10-15%)

- phosphatidylserine (PS; membrane fraction: 5-10%)
- phosphatidic acid (PA; membrane fraction: 1-2%); PA has no alcohol component

Further membrane components are cholesterol (CH; 10-20%), sphingomyelin (SM; 5-10%) and cardiolipin (CL; 2-5%), which is a phosphatidylglycerin (PG)-derived component of the intracellular mitochondria membranes.

Phosphatidylcholine

Phosphatidylcholine (PC) gained from soya lecithin is most frequently used in topical preparations. It should be mentioned in this context that the INCI denomination "lecithin" still remembers its origin and is misleading since the term lecithin also refers to a substance with completely different physical properties. Lecithin is a natural, weak anionic emulsifier used in food industry for the preparation of mayonnaise, bakery improvers and chocolates, among others. By contrast, PC spontaneously forms spherical membranes (vesicles) which are in accordance with the former herbal cells in terms of size and shape.

Carriers – liposomes

The vesicles can encapsulate water-soluble substances in their interior but also integrate lipophilic substances in the membranes. The resulting dispersions, discovered for the first time in the sixties³, do not require emulsifiers. Different versions have later on been used for the liposomes technology^{4,5}.

In contrast to the initial thinking that liposomes cannot only penetrate into the skin but also permeate through the skin, it could subsequently be proved that liposome membranes only fuse with the intercellular membrane structure of the stratum corneum and thus improve the penetration. In this process the phase transition temperature of the skin barrier or in other words, the transition from the less permeable coherent lamellar gel phase⁶ into a more permeable liquid-crystalline phase is lowered. The phase transition temperature of soya PC is below 0°C due to the high content

of essential fatty acids.

Lamellar base creams

By hydrogenating essential fatty acids into saturated fatty acids, this particular property of soya PC is lost. Hydrogenated phosphatidylcholine (INCI: hydrogenated lecithin), albeit in combination with sterines (cholesterol, phytosterines) and ceramides can, figuratively speaking, be used as a filler for the interrupted gel phase membranes of the horny layer⁷ in the case of dry skin since the phase transition temperature of about 42°C is close to the transition temperatures of the stratum corneum⁸. In technical terms, we speak of lamellar base creams with derma membrane structure. They are used for skin protection and skin care purposes and are characterized by an extremely low washout effect compared to conventional emulsions. The term washout-effect means the loss of cream- and skin barrier components during body cleansing – already when using plain water.

Nanodispersions

Since liposomes have a limited absorption capacity for lipophilic substances, biodegradable nanodispersions have been developed with particles of similar size which are surrounded by single instead of double mem-

branes. Phosphatidylcholine nanoparticles are liquid and suited for the encapsulation and application of essential fatty acids (linoleic acid, alpha- and gamma-linolenic acid) in the form of linseed-, kiwi- and evening primrose oil, as well as lipophilic vitamins and their derivatives. Nanodispersions also improve the penetration of encapsulated active agents.

Troubleshooters

The carriers (liposomes, nanodispersions) consisting of PC themselves are a very effective active agent and suited for the treatment of acne⁹ (15-lipoxygenase-substrate¹⁰) and of barrier disorders (ceramide I-substrate¹¹) due to their high fraction of bound linoleic acid and the low content of alpha-linolenic acid. Since the PC of the epidermis and the sphingomyelins (SM) – participating in the composition of membranes, as mentioned above – are in balance from which then ceramides develop during the apoptosis of skin cells, the skin will regenerate and improve after a topical application of external PC.^{12,13}

The following overview shows typical combinations of PC with active agents. The indications listed refer to therapy (dermatological) and supportive prevention (cosmetic) respectively the adjuvant skin care.

PC carrier	Active agent	Indication	Mode of action
liposomes	ascorbyl phosphate (vitamin C)	anti-aging, hyperpigmentation	collagen synthesis↑, tyrosinase inhibition, radical scavenger ^{14,15}
liposomes	azelaic acid (according to the German Federal Institute for Risk Assessment (BfR) ¹⁶ up to 1%)	acne, rosacea, perioral dermatitis	5-alpha-reductase-inhibitor (bacteria) ¹⁷
nanodispersion	boswellic acids	acne, rosacea, inflammation	protease-inhibitor ¹⁸
nanodispersion	coenzyme Q ₁₀	anti-aging	radical scavenger ¹⁵ , lipid metabolism↑
liposomes	caffeine	cellulite	lipolysis ¹⁹ , microcirculation↑
liposomes	Euphrasia Officinalis extract	eye care	eyebright (also angel's eye, bird's eye) – popular medicine
liposomes	fumaric acid	psoriasis	drug fumitory (also earth smoke, common fumitory) – popular medicine
liposomes	hyaluronic acid (combination, not encapsulated)	anti-aging	skin hydration↑, wrinkle reduction
liposomes	isoflavones	anti-aging	local estrogenic effects ²⁰
liposomes	Kigelia africana fruit extract	anti-aging	skin tightening
nanodispersion	kiwi oil	burns, sun burn, inflammation	15-lipoxygenase-substrate ²¹
liposomes	Laminaria digitata (wakame, also oar kelp)	anti-aging	skin hydration↑, wrinkle reduction
nanodispersion	linseed oil	burns, sun burn, inflammation	15-lipoxygenase-substrate ²¹
nanodispersion	evening primrose oil	neurodermitis, inflammation	15-lipoxygenase-substrate, substitute in the case of a delta-6-desaturase-defect ²¹
liposomes	NMF (amino acids)	anti-aging	skin hydration↑, radical scavenger ²²
liposomes	proanthocyanidin (OPC)	anti-aging	radical scavenger ¹⁵
nanodispersion	retinol acetate or retinyl palmitate (vitamin A)	anti-aging, acne	regeneration ¹⁴ , collagen synthesis↑

PC carrier	Active agent	Indication	Mode of action
liposomes	sphingosin-1-phosphate	psoriasis	Inhibition of keratinocyte proliferation ²³
liposomes	spilanthol	anti-aging	wrinkle reduction through muscle relaxation ²⁴
nanodispersion	tocopherol acetate (vitamin E)	anti-aging, skin protection	radical scavenger ¹⁵ , regeneration ¹⁴
liposomes	tranexamic acid	hyperpigmentation, rosacea	tyrosinase inhibition, anti-fibrinolysis ²⁵
liposomes	niacinamide (vitamin B ₃)	anti-aging	regeneration ¹⁴ , anti-inflammatory
liposomes	zinc salts	acne	component of oxidoreductases ²¹

The choline fraction (2-hydroxyethyl-trimethylammonium salt) of PC and SM is the base substance for acetylcholine, a neurotransmitter, which is essential for brain and nerve functions.^{26,27} In addition, choline is a significant methyl group donor in the human metabolism.

Phosphatidylcholine-based oleogels

PC is easy to integrate into the lamellar barrier layers of the skin, a property which is also used in the context of mineral oil free oleogels. The products are non-aqueous and have a content of more than 90% of herbal lipids and fatty acids. Despite their high lipid content, the oleogels have an excellent penetrability and can be used for the care of atopic skin, for infantile skin care and, when formulated with appropriate active agents, also for the care of rosacea skin. Since there is no water phase which has to be stabilized with cosmetic additives such as emulsifiers and preservatives, tolerance problems as for instance allergies or irritations are virtually excluded. Further medical indications are perioral dermatitis, perianal barrier disorders, diabetic skin and decubitus (bet sores).²⁸

Phosphatidylserine

Phosphatidylserine (PS) belongs to the vital phospholipids²⁹ and is found in the interior part of the bilayered cell membrane of herbal and animal cells. With apoptosis or in other words, the programmed cell death, PS enzymatically finds its way to the outward part of the membrane. This is a signal for macrophages (the scavenger cells or phagocytes of the immune system) to encircle and digest the respective cells³⁰. With injuries and the thus related blood coagulation, phosphatidylserine also ends up at the cell surface and accelerates the blood coagulation.³¹ Since it activates the macrophages and the blood coagulation, phosphatidylserine has an anti-inflammatory effect.^{32,33} In this context, also neuroprotective³⁴, antioxidative³² effects, and the inhibition of UV-in-

duced procollagen degradation and MMP-1³⁵ formation are discussed.³⁶

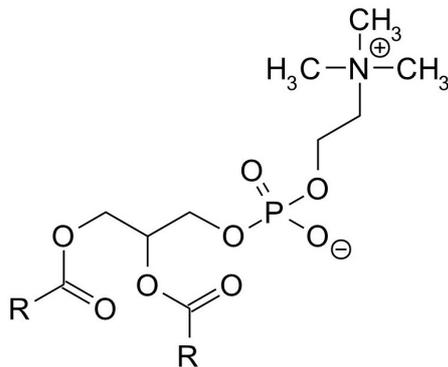
When hydrogenated phosphatidylcholine is substituted by unsaturated phosphatidylserine (PS), lamellar creams are converted into water-in-oil emulsions (W/O). Since phosphatidylserine is a physiological substance and perfectly fits into the natural phospholipid balance of the body, these emulsions do not cause washout effects. The contrary is the case: the emulsions have an excellent adhesiveness and the transepidermal water loss (TEWL) can be reduced with the processed lipid substances. The creams have anti-inflammatory effects due to phosphatidylserine as messenger but also due to the chemically bound essential fatty acids in phosphatidylserine. Similar to the unsaturated soya phosphatidylcholine, the latter mentioned are released in the skin through the phospholipases A₁ and A₂ and subsequently converted into anti-inflammatory metabolites through 15-lipoxygenase (15-LOX).^{37,10} Phosphatidylserine creams can be used for skin protection purposes, in the case of eczema, light sun erythema and for the care of the atopic skin. Interesting fact: higher concentrations of phosphatidylserine occur in cold water fish (herring, mackerel) and in the cerebral matter.³⁸ PS-enriched extracts are sold as food supplements. With calcium salts, phosphatidylserine forms tubular structures (cochleates) that, in nanoscale, are suitable carriers for pharmaceutical drugs.³⁹

Synthetic phospholipids

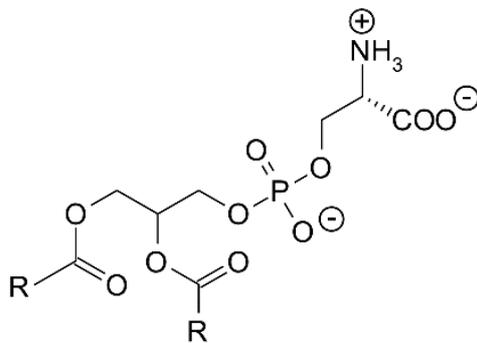
The properties of natural phospholipids are the basis for a multitude of synthetic variants used as liposome base substances. Their purpose is a modified degradation of the carriers and the controlled availability of pharmaceutical drugs in different routes of administration (topical, intravenous, oral).

Figures

Structural formula of phosphatidylcholine



Structural formula of phosphatidylserine



Dr. Hans Lautenschläger

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