PHYTOSPHINGOSINE SLC

Novel Sphingolipid derivative with unique anti-ageing properties

- Proven benefits for both chronologically aged and photoaged skin
- Smoothes the skin's appearance by reducing deep wrinkles
- Induces pro-collagen synthesis in the dermis and reduces undesired collagen degradation
- Reinforces the dermal-epidermal junction (DEJ) of the skin
- Improves the barrier function of the skin from within by supporting epidermal cell differentiation
- Reduces symptoms of inflamed skin
- Active at low concentration

Personal Care

INCI-Name (CTFA-Name)

Salicyloyl Phytosphingosine

Chemical and physical properties (not part of the specification)

Form	Off-white powder
Melting point [°C]	Approx. 105

Phytosphingosine SLC is a derivative of the naturally occurring skin-identical Phytosphingosine which is covalently coupled with salicylic acid.
Phytosphingosine SLC is of the highest quality and purity and is patent protected (EP 966431).

Properties

Skin aging is the combination of chronological aging (simply getting older) and photoaging (premature skin aging due to the effects of cumulative exposure to UV radiation). As skin ages, its structure and chemistry are altered. For instance, the cell movement from the bottom of the epidermis to the top (cell differentiation) becomes slower. In the dermis, UV radiation breaks down collagen and elastic fibers leading to visible wrinkles. From a clinical point of view, skin becomes dry and thinner, it looses its elasticity, firmness and softness causing wrinkles to appear.

Phytosphingosine SLC contributes to minimizing the signs of aging by:

- Supporting epidermal cell differentiation, skin repair and skin renewal
- Improving the conditions of mature or photo-aged dermis by boosting collagen synthesis and reducing its degradation
- Reinforcing the dermal-epidermal junction
- Soothing inflamed skin

Efficacy studies

- ***DNA-Chip Technology, ESI-MS Analysis***

Studies were performed at the University of Regensburg (1).

The effect of Phytosphingosine SLC on broad gene expression was analyzed via DNA-chip technology in human primary keratinocytes.
With the help of DNA-chip technology a comparison of gene expression patterns allows a qualitative estimation on effectiveness.
Therefore, primary keratinocyte cell cultures were incubated with 5 µM Phytosphingosine SLC and cultivated over 96 hours (= 4 days). On day 2 and 4 RNA of cell cultures was prepared. It was demonstrated that related to the control, Phytosphingosine SLC changed the regulation of more than 300 genes with a factor >2.5 fold either one or four days after exposure. The pattern of the affected genes showed, on the one side, an induction of genes responsible for cell growth and differentiation. On the other side, a repression of genes responsible for inflammation was observed.

Additionally to the gene expression patterns, metabolite analysis was performed. The lipid content of human primary keratinocytes was assessed by electrospray ionization tandem mass spectrometry (ESI-MS/MS).

Therefore, the composition of the cellular lipid phase of the cultured keratinocytes was determined. It was shown that Phytosphingosine SLC significantly induced an increase in the total ceramide content (Data not provided).

- ***Influence on stratum corneum lipid synthesis (SkinEthic™)***

The study was performed at Degussa, Stockhausen GmbH & Co. KG, Laboratory for Toxicology and Ecology (2).

The efficacy of Phytosphingosine SLC to increase ceramide production in the epidermis was estimated on an artificial skin model. A cosmetic O/W formulation containing 0.2 % of Phytoshingosine SLC was topically applied to the 3D skin model. After 24 h of incubation lipids were analyzed via TLC analysis.

Figure 1 demonstrates that Phytosphingosine SLC increases the ceramides levels necessary for lipid barrier formation. Especially the amount of Ceramide 9 which is crucial for the lipid layer cohesion was enhanced effectively by the influence of Phytosphingosine SLC.

The benefits on the skin barrier function were confirmed by *in vivo* measurements where Phytosphingosine SLC showed a significant decrease in the TEWL (Data not provided).

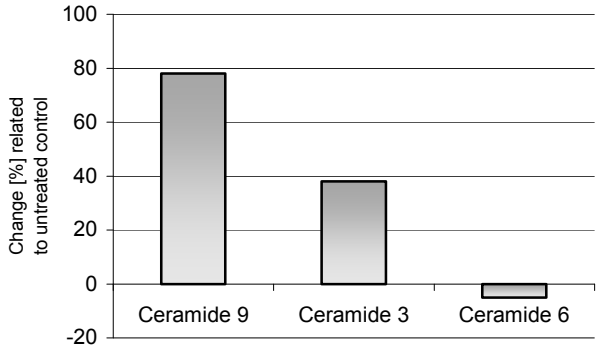

Fig. 1: Change of ceramide content in a 3D Skin model (SkinEthic™)

Phytosphingosine SLC enforces the formation of the total *stratum corneum* barrier from within.

- ***Skin biopsies: Repair of photoaged skin***

The study was performed at the Dermatology Center, Hope Hospital, Manchester (UK) (3).
Five healthy but clinically photoaged volunteers were recruited for the performance of the study.

Test substances (Vehicle, 0.2 % Phytosphingosine SLC, and 0.025 % all-*trans* retinoic acid as a positive standard) were applied separately under occlusive patch (6 mm Finn chambers) to the forearm. Test formulations were applied to clean skin on days 1 and 4 except all-*trans* retinoic acid which due to potential side effects was applied on day 4 only. On day 8, Finn chambers were removed and 3 mm punch biopsies were obtained from each test site. Biopsy sections were frozen and finally prepared for immunohistochemistry. The degree of immuno staining was assessed with a semi-quantitative score (0 = no staining; 4 = maximal staining). Three proteins known to be altered in photoaged skin were assayed (Fibrillin, procollagen-1 and matrix metalloprotease 1 (MMP 1)) to evaluate the benefits of Phytosphingosine SLC on skin aging.

- *Fibrillin*

The distribution of fibrillin-rich microfibrils proximal to the dermal-epidermal junction (DEJ) is reduced by photoaging.
The efficacy of Phytosphingosine SLC to increase the genetic fibrillin expression was already proven by DNA chip technology.
The effect on the appearance of the microfibrils next to the DEJ was now investigated and compared to the "golden standard" all-*trans* retinoic acid which is known to increase the fibrillin expression.
Fig. 2 shows typical immunohistochemical images (Magnification 40x). The figure demonstrates that the application of Phytosphingosine SLC increases by 82 % fibrillin 1 synthesis and a reinforcement of the fibrillin-filled microfibrils down from the DEJ was observed (See arrows).

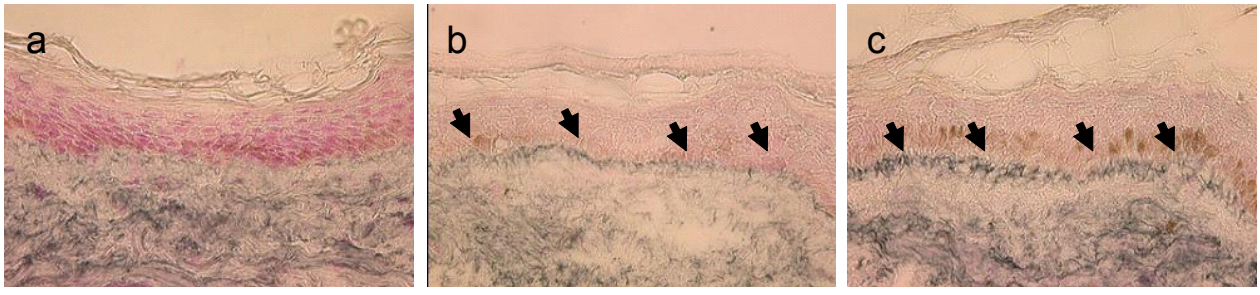

Fig. 2: Fibrillin 1, immunohistochemistry

a: Vehicle; b: 0.2 % Phytosphingosine SLC; c: 0.025 % all-*trans* retinoic acid

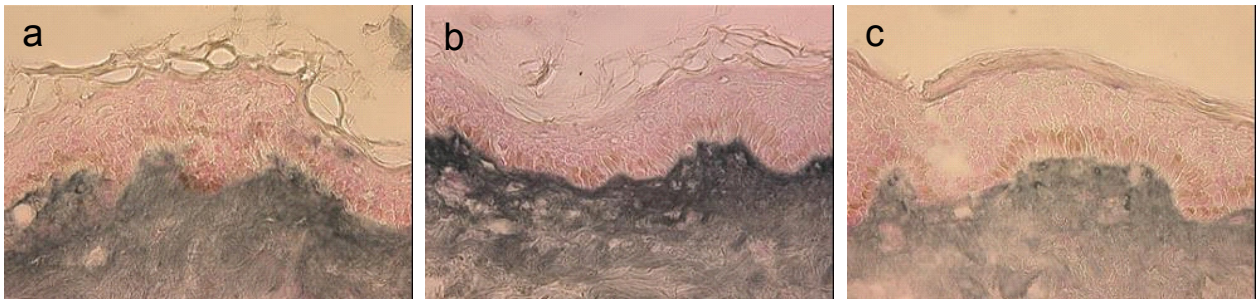

Fig.3: pro-Collagen I, immunohistochemistry
a: Vehicle; b: 0.2 % Phytosphingosine SLC; c: 0.025 % all-trans retinoic acid

- *Pro-collagen I*

The amount of the different collagen types, especially type I and III, and their precursors decrease during aging and as a consequence the skin looses its firmness and elasticity causing wrinkles to appear.
Figure 3 shows the immunohistochemical images of the skin section regarding pro-collagen I, a precursor of collagen I. The grey staining of the papillary dermis demonstrates that Phytosphingosine SLC increases the pro-collagen I content by 30 % whereas all-*trans* retinoic acid only showed little effect in this short-term study.

- *Matrix metalloprotease I (MMP I)*

MMP's or collagenases are dermal enzymes cleaving collagen strings and therefore accelerating symptoms of aging by reducing the amount of collagens in the dermis.
Figure 4 indicates that the application of Phytosphingosine SLC reduced the amount of the matrix metalloprotease 1 in the dermis by 46 %. In contrast, the application of all-*trans* retinoic acid had no effect on the MMP I expression in the short-term study.

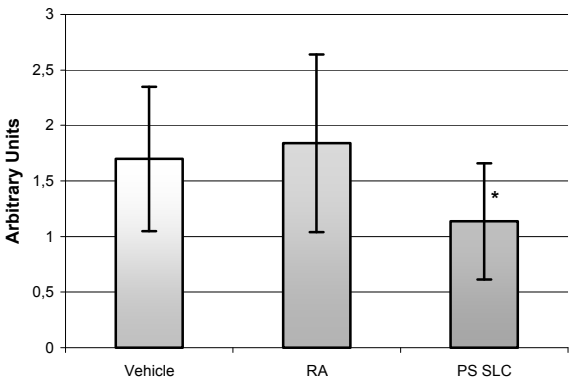

Fig. 4: Reduction of MMP I expression after application of Phytosphingosine SLC

In summary, the skin biopsies demonstrate that Phytosphingosine SLC is able to restore both the fibrillin-rich microfibrillar network and the dermal pro-collagen I amount. Furthermore, Phytosphingosine SLC reduces the amount of MMP I and therefore supports the dermal matrix consisting mainly of collagen I.

- ***In vivo study: Anti-wrinkles effect***

The study was performed at the Institute Dr. Schrader, Holzminden (D) (4).
Thirty volunteers were recruited for the performance of the study.

To confirm the skin firming effect of Phytosphingosine SLC due to its supporting efficacy in the dermis and at the DEJ, an *in vivo* study with the FOITS equipment was accomplished. The "Fast optical in vivo topometry of human skin" is a non-contact method to measure the three-dimensional profile of skin areas and therefore to estimate the influence of active ingredients on wrinkles.

The volunteers applied twice daily an O/W cream without (vehicle) and with 0.2 % Phytosphingosine SLC (active cream) during a period of four weeks to their periorbital areas of the face (half-side test). Phytosphingosine SLC significantly reduced the wrinkle depth of the skin as observed with 10 % decrease of the macro-structure. Which results in the skin becoming more even.
These benefits, together with the significant decrease of the skin roughness (Ra and Rz parameters, data not provided) were visualized by a photographical analysis of the skin structure before and after application (See therefore Fig. 5 and 6).

In conclusion, Phytosphingosine SLC is an ideal active ingredient to prevent and reverse the signs of skin aging.

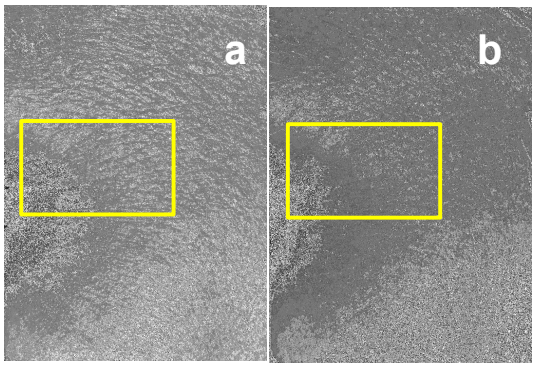

Fig. 5: Representative case study
a: Before application of Active cream
b: After 4 weeks

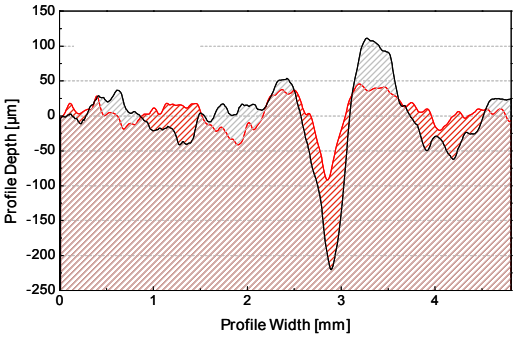

Fig. 6: Analysis of skin structure
Black: Baseline
Red: After 4 weeks

References

(1) Final study report, University of Regensburg, November 2003

(2) Final study report, Degussa, Stockhausen GmbH & Co. KG, Laboratory for Toxicology and Ecology, July 2004

(3) Final study report, Dermatology Center, Hope Hospital, Manchester (UK), May 2005

(4) Final study report, Institute Dr. Schrader, August 2005

Efficacy studies are available on request.

Application

Phytosphingosine SLC was designed to be used in the following Skin Care products:

- Anti-aging formulations
- Anti-wrinkles and firming formulations
- Skin renewal and repair formulations
- Skin soothing formulations
- After sun products

Preparation of emulsions

Phytosphingosine SLC is an amphiphilic molecule and can be readiliy incorporated into the lamellar liquid crystalline phases of cosmetic O/W emulsions.

An outstanding solubility in low molecular weight alcohols, broadens the formulation utility.

Processing hints for emulsions: Phytosphingosine SLC must be clearly solubilized in the hot oil phase, and the temperature of oil and water phase should be high enough to ensure that the Phytosphingosine SLC does not recrystallize during the homogenization step. Depending on the composition of the oil phase, the temperature should be around 70-90°C. Choosing emollients with a good solvency for Phytosphingosine SLC, e. g. VARONIC® APM (PPG-3 Myristyl Ether), TEGOSOFT® TN (C12-15 Alkyl Benzoate) and TEGOSOFT® CT (Caprylic/Capric Triglyceride), and prolonging the heating time facilitates the formation of clear Phytosphingosine SLC solutions. To obtain a pleasant skin feel it is suggested to combine those emollients with low viscosity emollients such as TEGOSOFT® OP (Ethylhexyl Palmitate), TEGOSOFT® DC (Decyl Cocoate) or TEGOSOFT® DEC (Diethylhexyl Carbonate).

Packaging

0.10 kg small size
1.25 kg standard size

Suggested use concentration

0.05 % - 0.2 % Phytosphingosine SLC

Hazardous goods classification

- Information concerning
- classification and labelling according to regulations for transport and for dangerous substances
- protective measures for storage and handling
- measures in accidents and fires
- toxicity and ecological effects

is given in our material safety data sheets.

Guideline Formulations

Anti-Wrinkle Facial Cream WR 16/01-105	
Phase A	
ABIL® Care 85 (Bis-PEG/PPG-16/16 PEG/PPG-16/16 Dimethicone; Caprylic/Capric Triglyceride)	1.00 %
TEGIN® (Glyceryl Stearate SE)	4.00 %
TEGO® Alkanol 1618 (Cetearyl Alcohol)	3.00 %
Stearic Acid	0.50 %
Cyclomethicone	10.00 %
TEGOSOFT® TN (C12-15 Alkyl Benzoate)	3.00 %
VARONIC® APM (PPG-3 Myristyl Ether)	3.30 %
Phytosphingosine SLC	0.20 %
Phase B	
Glycerin	3.00 %
Water	70.82 %
Phase C	
Sodium Hydroxide (10 % in water)	0.43 %
Phase D	
TEGO® Carbomer 134 (Carbomer)	0.15 %
TEGOSOFT® OP (Ethylhexyl Palmitate)	0.60 %
Preservative, Perfume	q.s.

Preparation:

1. Heat phase A and B separately to approx. 80°C.
2. Add phase A to phase B with stirring. [1)]
3. Homogenize.
4. Cool with gentle stirring to approx. 70°C and add phase C with gentle stirring.
5. Add phase D at approx. 60 °C and homogenize for a short time.
6. Cool with gentle stirring below 30°C.

[1)] Important: If phase A has to be charged into the vessel first, phase B must be added **without stirring**.

Soothing Day Cream for Mature Skin WR 3/04-2c	
Phase A	
TEGO® Care 450 (Polyglyceryl-3 Methylglucose Distearate)	3.00 %
TEGIN® M Pellets (Glyceryl Stearate)	2.50 %
TEGO® Alkanol 18 (Stearyl Alcohol)	1.50 %
TEGOSOFT® CT (Caprylic/Capric Triglyceride)	3.30 %
TEGOSOFT® TN (Caprylic/Capric Triglyceride)	4.00 %
VARONIC® APM (PPG-3 Myristyl Ether)	4.00 %
TEGOSOFT® DEC (Diethylhexyl Carbonate)	1.00 %
Tocopheryl Acetate	0.50 %
Phytosphingosine SLC	0.20 %
Phase B	
Glycerin	3.00 %
Allantoin	0.10 %
Panthenol	0.50 %
Water	74.4 %
Phase C	
TEGO® Carbomer 134 (Carbomer)	0.20 %
TEGOSOFT® TN (Caprylic/Capric Triglyceride)	0.80 %
Phase D	
Sodium Hydroxide (10 % in water)	q.s.
Phase E	
LACTIL® (Sodium Lactat; Sodium PCA; Glycine; Fructose; Urea; Niacinamide; Inositol; Sodium Benzoate; Lactic Acid)	0.15 %

Preparation:

1. Heat phase A and B separately to approx. 80°C.
2. Add phase A to phase B with stirring. [1)]
3. Homogenize.
4. Cool with gentle stirring to approx. 60°C and add phase C.
5. Homogenize for a short time.
6. Cool with gentle stirring and add phase D/E below 40°C.

[1)] Important: If phase A has to be charged into the vessel first, phase B must be added **without stirring**.

Skin Firming Body Milk **WR 3/04-15a**	
Phase A	
ISOLAN® GPS (Polyglyceryl-4 Diisostearate/ Polyhydroxystearate/ Sebacate)	3.00 %
Hydrogenated Castor Oil	0.25 %
Paracera M (Microcristalline Wax, Paramelt B.V.)	0.25 %
TEGOSOFT® TN (C12-15 Alkyl Benzoate)	10.7 %
TEGOSOFT® DEC (Diethylhexyl Carbonate)	10.0 %
Tocopheryl Acetate	0.60 %
Phytosphingosine SLC	0.20 %
Phase B	
Glycerin	3.00 %
GluCare® S (Sodium Carboxymethyl Betaglucan)	0.20 %
TEGO® Cosmo C 100 (Creatine)	0.50 %
D-Panthenol (Panthenol, Roche Vitamins)	0.50 %
Magnesium Sulfate Heptahydrate	1.00 %
Water	69.8 %
Phase Z	
Preservative, Perfume	q.s.

Preparation:

1. Heat phase A to approx. 80°C.
2. Add phase B (80°C or room temperature) slowly while stirring.
3. Homogenize for a short time.
4. Cool with gentle stirring below 30°C and homogenize again.

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Especially concerning Active Ingredients

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