SPHINGOKINE® NP

The Multilayer Approach to Facial Contouring

- Reduces the appearance of skin sagging
- Appears to plump and firm the skin
- Helps prevent and slow the look of aging
- Reduces the visibility of wrinkles
- Skin feels tighter and better toned
- Usage concentration: 0.02– 0.2%

Personal Care

INCI name (PCPC name)

Caprooyl Phytosphingosine

Chemical and physical properties (not part of specifications)	
Form	powder
Active matter	≥ 90%

Introduction

The skin, as the largest human organ, functions as a mechanical and chemical protective barrier between the body and the environment. It is composed of different layers, the outermost epidermis with the main barrier function and the subjacent dermis. Below the dermis, the hypodermis, or subcutaneous tissue, is located. Communication between cells within a certain skin layer, across different skin layers, and between different skin cell types is very important for the proper function of skin. This communication takes place via multiple types of cell signalling molecules: petide hormones such as adiponectin and leptin, cytokines such as growth factors, and sphingolipids such as ceramideswhich are capable of controlling the action of the surrounding tissue. The concept that ceramides and phospholipids can function as more than cell membrane structural components or sources of energy via metabolism, has been the source of much recent research. Results have revealed that short-chain ceramides are crucial signalling molecules involved in cellular proliferation, differentiation, and apoptosis.

In vitro studies and proposed mechanism

The unique short-chain ceramide SPHINGOKINE® NP contains skin identical stereochemistry to natural skin ceramides. It was tested *in vitro* and the potential for cellular cross-talk was measured(data available upon request). Results indicate that SPHINGOKINE® NP may provide an avenue to improving communication between skin cells (Figure 1).

Our results in keratinocyte culture, lead us to propose that SPHINGOKINE® NP may improve keratinocyte differentiation, which may then lead to strengthening, firming and smoothing of the *stratum corneum*, resulting in a more effective barrier protecting the inner layers of human skin.

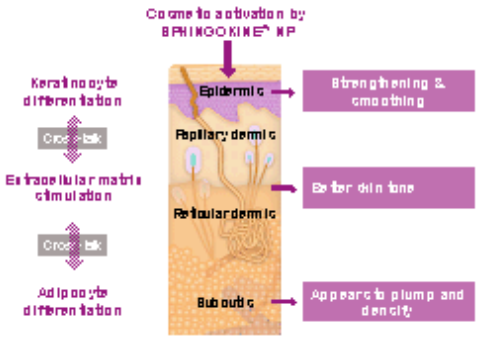

Figure 1: Proposed mechanism of SPHINGOKINE® NP

In addition, more effective communication between epidermal keratinocytes and fibroblasts may result in the improved appearance and organization of the extracellular matrix (ECM). Further, improved communication across all layers of skin, may also result in dermal matrix formation stimulated by keratinocyte- and adipocyte-derived signals.

SPHINGOKINE® NP-induced cross-talk may also result in additional support of the dermal ECM due to stimulation of lipogenesis which then results in denser subcutaneous fat tissue. This effect manifests as visibly plumped and reshaped skin.

Facial cosmetic consumer panel study

Appearance of skin sagging and wrinkle depth

Caucasian women (aged 50-70 years) participated in this study. Both formulations, one containing 0.2% SPHINGOKINE® NP and the vehicle formulation were each tested by 30 volunteers in a half-side test. The formulations were applied twice daily on the face. The skin measurements were carried out at the beginning and after 4, 8, and 12 weeks in temperature and humidity-controlled rooms (24 ± 2°C, 50 ± 10% relative humidity). The following parameters have been evaluated: skin roughness (wrinkle depth), skin density/echogenicity, the sagging degree of the skin. Finally digital images have been taken.

Treatment with SPHINGOKINE® NP decreased the appearance of skin sagging significantly after 8 weeks and the effect was maintained by extended application through the 12-week test period.

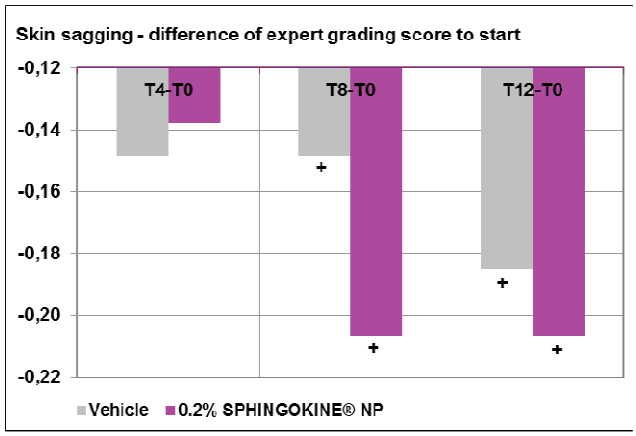

Figure 2: Appearance of skin sagging relative to the beginning after 4, 8, and 12 weeks of application of SPHINGOKINE® NP graded by experts. (Statistics: Student's t-test + p<0.05 vs. start).

The reduced appearance of sagging skin following the application of SPHINGOKINE® NP can also be seen in the digital images (figure 3).

(a) (b)

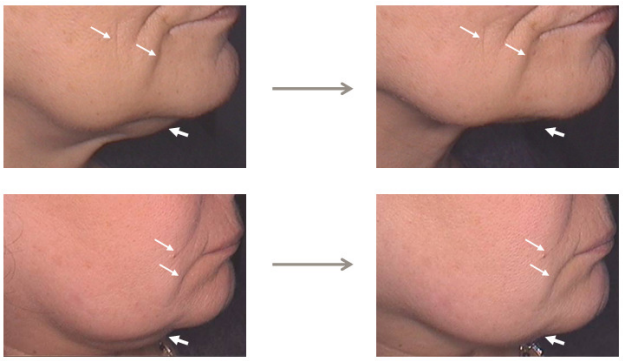

Figure 3: Digital images of two representative volunteers. (a) before, (b) 12 weeks after application of 0.2% SPHINGOKINE® NP.

The sagging skin regions in the chin area have been improved and the contour of the face appears visibly lifted. In addition, it can be seen that the depth of oral commissures and smile lines in the area at the mouth also appear reduced by SPHINGOKINE® NP.

These observations can be further substantiated by measuring skin echogenicity/skin density. After 8 weeks application of the formulation containing 0.2% SPHINGOKINE® NP, compared to the vehicle, skin echogenicity/skin density appears to be markedly improved (Figure 4). The improvement becomes significant after 12 weeks.

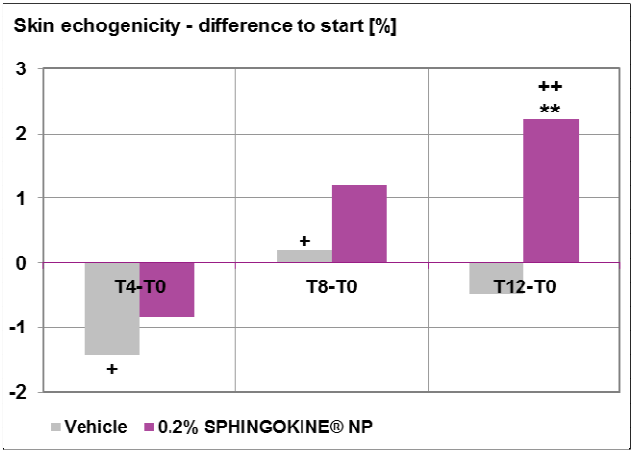

Figure 4: Skin echogenicity/skin density relative to the beginning after 4, 8, and 12 weeks of application of SPHINGOKINE® NP. (Statistics: Student's t-test ++ p<0.01, + p<0.05 vs. start; ** p<0.01 vs. vehicle).

An example picture taken from the ultrasound scanner illustrates these results. The images show ultrasound pictures of the skin at the defined time points. The lighter the structures appear, the denser is the skin tissue. Following the application of SPHINGOKINE® NP, skin structure appears to be improved, and skin feels more toned and firmer.

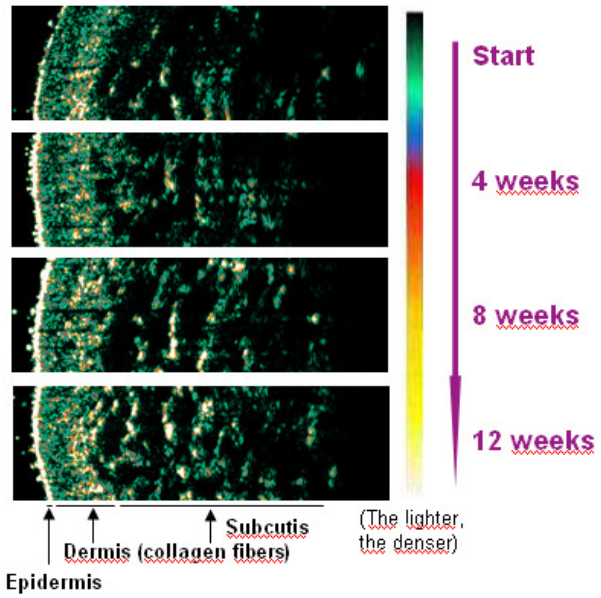

Figure 5: Skin image from one panelist

Appearance of skin surface

Application of SPHINGOKINE® NP led to a decrease in the appearance of skin roughness (Figure 6). This effect was statistically significant compared to the vehicle control after 8 weeks of application. After 12 weeks, about 5-fold improvement in the appearance of wrinkle depth, compared to the vehicle formulation, could be observed.

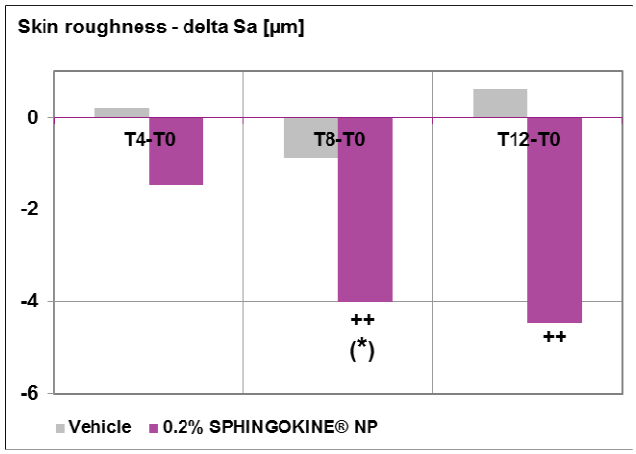

Figure 6: Appearance of skin surface roughness (Sa)/wrinkle depth relative to the beginning after 4, 8, and 12 weeks of application of SPHINGOKINE® NP. (Statistics: Student's t-test ++ p<0.01 vs. start; ** p<0.01, (*) p<0.1 vs. vehicle).

These effects can also be observed in the PRIMOS Pico images (Figure 7). The depth of the wrinkles near the eye appear visibly reduced 12 weeks after application of 0.2% SPHINGOKINE® NP.

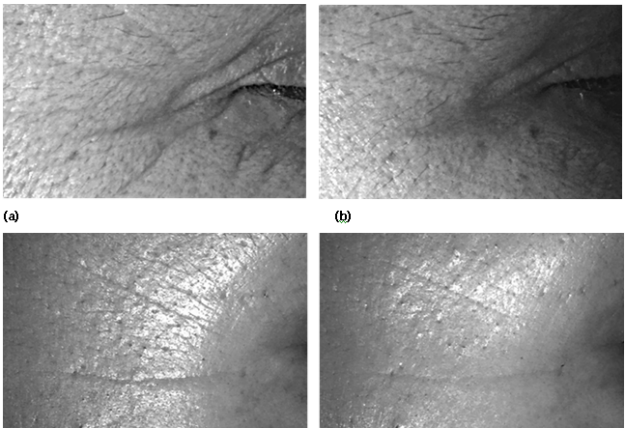

Figure 7: PRIMOS Pico images of two representative volunteers. (a) before, (b) 12 weeks after application of 0.2% SPHINGOKINE® NP.

Upper arm cosmetic consumer panel study

Appearance of upper arm skin sagging

The aim of this study was to evaluate dose-dependent effects of SPHINGOKINE® NP in the appearance of the signs of gravitational aging on upper arm skin.

Caucasian women (aged 50-70 years) participated in this study. The test formulations containing 0.02% SPHINGOKINE® NP, 0.05% SPHINGOKINE® NP and the vehicle formulation were each tested by 16 volunteers in a half-side test. The side of application of the product (right or left arm) was randomized among the subjects. The formulations were applied twice daily on the areas between the armpits and the elbows for 8 weeks. Skin density/echogenicity was assessed with an ultrasound scanner.

Apparent changes in skin firmness and tone, via ultrasound measurement, on the upper arm after 4 and 8 weeks of treatment with SPHINGOKINE® NP were observed (Figure 8).

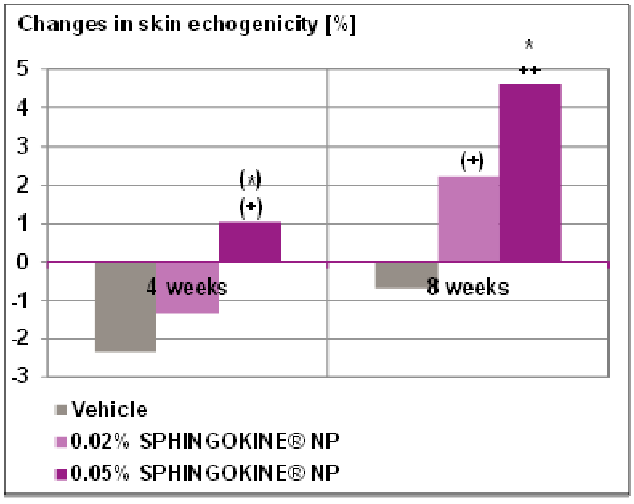

Figure 8: Skin echogenicity/skin density measurements of upper arm skin compared to starting values after 4 and 8 weeks of application of SPHINGOKINE® NP.

It can be observed that the vehicle formulation does not have a significant effect on the appearance of skin density over the study period, and neither does the test formulation containing the 0.02% SPHINGOKINE® NP after four weeks of treatment. However, in case of 0.05% SPHINGOKINE® NP, after four weeks, significant changes, compared to starting value and also compared to vehicle treatment were observed. This improvement in the appearance of skin tone and firmness was much more pronounced after eight weeks of treatment up to almost 5%. At that point in time, also treatment with 0.02% SPHINGOKINE® NP showed a significant effect compared to starting conditions of around 2% improvement. Overall, it could be shown that SPHINGOKINE® NP has an in vivo efficacy in improving the appearance of skin tone and firmness at relatively low concentrations. Skin echogenicity on the upper arm, which is correlated with the appearance of upper arm sagging, was significantly improved. The result of this study suggests a usage concentration of 0.02-0.05% for body care applications

The results of this study demonstrate that SPHINGOKINE® NP improves the appearance of signs of gravitational aging on human skin. SPHINGOKINE® NP provides a multilayer approach which has been shown in various *in vitro* studies on different skin cells. It is thought to improve keratinocyte-fibroblast and adipocyte-fibroblast cross-talk, thereby, providing a potentially stronger and firmer scaffold leading to skin which appears plumped and toned. These effects lead to reduced appearance of skin sagging, and wrinkles that are perceptually less deep.

Taken together, SPHINGOKINE® NP is an innovative active ingredient for different kinds of anti-aging applications like anti-sagging products, shaping creams for face and body and products for improving the appearance of facial contours.

A detailed test summary report (technical dossier) is available on request.

Claim summary

- Reduces the appearance of skin sagging
- Helps prevent the look of aging
- Appears to plump and firm the skin
- Visibly slows the appearance of the signs of aging
- Wrinkle depth appears reduced
- Skin feels tighter and better toned

Patent position

A patent application describing the use of SPHINGOKINE® NP in cosmetic formulations for reduction of skin sagging was filed by Evonik Industries AG.

To the best of our knowledge, there are no 3rd party rights covering the usage of SPHINGOKINE® NP in cosmetic formulations.

Formulation hints

SPHINGOKINE® NP is best soluble in polar oils like TEGOSOFT® G 20 and TEGOSOFT® APM or in solubilizers like pentylene glycol. Therefore, it is recommended to substitute a part of the oil phase by these polar oils.

For cold processed emulsions it is recommended to solubilize SPHINGOKINE® NP in pentylene glycol.

Preparation of an O/W emulsion (cream or lotion):

SPHINGOKINE® NP is added to the oil phase of the emulsion which has to be heated to 75-80 °C until SPHINGOKINE® NP is completely solubilized. Then the emulsion is prepared as usual. The emulsion viscosity can be adjusted by using hydrocolloids like carbomer (TEGO® Carbomer types) or xanthan gum.

Preparation of a W/O emulsion (cream or lotion):

SPHINGOKINE® NP is added to the oil phase of the emulsion and heated up to 75-80°C until it is completely solubilized. Then the emulsion is prepared as usual.

Recommended usage concentration

0.02 - 0.2%, clinically tested at different concentrations

Possible applications

- Anti-aging face care
- Anti-sagging products
- Facial contour products
- Shaping creams and lotions

Packaging

0.25 kg

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.

Guide Line Formulations

Strengthening and Firming Body Lotion (MM 222/3)	
Phase A	
AXOL® C 62 Pellets (Glyceryl Stearate Citrate)	1.5%
TEGO® Alkanol 1618 (Cetearyl Alcohol)	1.0%
TEGOSOFT® CR (Cetyl Ricinoleate)	1.0%
TEGOSOFT® G 20 (Octyldodecanol)	6.0%
TEGOSOFT® DEC (Deiethylhexyl Carbonate)	5.5%
SPHINGOKINE® NP	0.1%
TEGO® Xymenynic (Caprylic/Capric Triglyceride; Xymenynic Acid)	2.5%
Phase B	
Glycerin	3.0%
Water	78.4%
Phase C	
TEGO® Carbomer 141 (Carbomer)	0.2%
TEGOSOFT® DEC (Diethylhexyl Carbonate)	0.8%
Phase D	
Sodium Hydroxide (10% in water)	q.s.
Phase Z	
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.. 60°C and add phase C.
5. Homogenize for a short time.
6. Cool with gentle stirring and add phase D below 40°C.

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

Volume Lifting Cream (MM 224/7)	
Phase A	
TEGO® Care PSC 3 (Polyglyceryl-3 Dicitrate/Stearate)	3.0%
TEGO® Alkanol 18 (Stearyl Alcohol)	1.3%
TEGIN® M Pellets (Glyceryl Stearate)	1.2%
TEGOSOFT® APM (PPG-3 Myristyl Ether)	8.5%
TEGOSOFT® OS (Ethylhexyl Stearate)	6.0%
TEGOSOFT® OER (Oleyl Erucate)	5.0%
SPHINGOKINE® NP	0.1%
Phase B	
Glycerin	3.0
Water	71.7
Phase C	
Keltrol CG-SFT (Xanthan Gum)	0.2%
Phase Z	
Preservative, Perfume	q.s.

Preparation:

1. Heat phase A and B separately to approx. 85°C
2. Add phase A to phase B with stirring 1).
3. Homogenize.
4. Cool with gentle stirring
5. Add phase C below 40°C

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

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