

TEGO® Stemlastin

Delaying chronological aging

Intended use

Active for skin care

Benefits at a glance

- Protects and maintains epidermal stem cell capacity for rejuvenated skin activity
- Boosts elastic fibers for highly supple skin
- Fights skin elasticity fatigue
- Retains a youthful appearance
- Usage concentration: 1 – 5%

INCI (PCPC Name)

Algae extract

Chemical and physical properties

(not part of specifications)

Form	aqueous solution
Active matter	approx. 2.5% dry matter based on algae biomass

Introduction

During the chronological aging process epidermal skin stem cells become less effective, meaning that the renewing and repairing activity of the epidermis is reduced. In addition to that, less and less elastic fibers are synthesized which induces a progressive loss of skin elasticity.

TEGO® Stemlastin, a standardized extract of the micro alga *Cyanidium caldarium* was found to have a combined activity on epidermal stem cells and elastic

fibers (Figure 1). TEGO® Stemlastin clearly retains a youthful appearance and reduces the signs of chronological aging.

TEGO® Stemlastin...

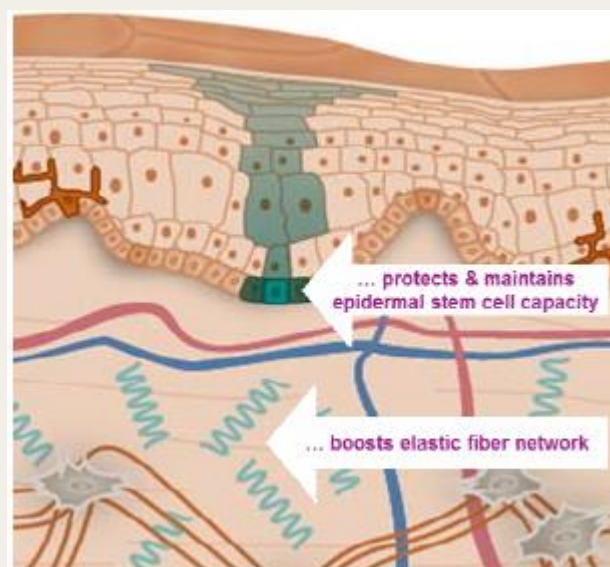


Figure 1 : Suggested working mechanism of TEGO® Stemlastin

The algae *Cyanidium caldarium* is able to survive under extreme environmental conditions. Therefore, the extract delivers a special intracellular composition of extremolytes like mineral nutrients, amino acids, algae polyphenols and is enriched in gamma amino butyric acid (GABA).

The strain that is used for the production of TEGO® Stemlastin was isolated on the Sunda Islands in Southeast Asia from mount Lawu fumaroles on the Java Island.

This production (Figure 2) of the bioactive algae extract TEGO® Stemlastin is a natural and ecofriendly process from biorenewables without external organic carbon sources. The cells grow only in the presence of light and nutrients. After cultivation the algae cells are processed by a proprietary mild extraction method followed by a filtration step enriching the bioactive compounds.

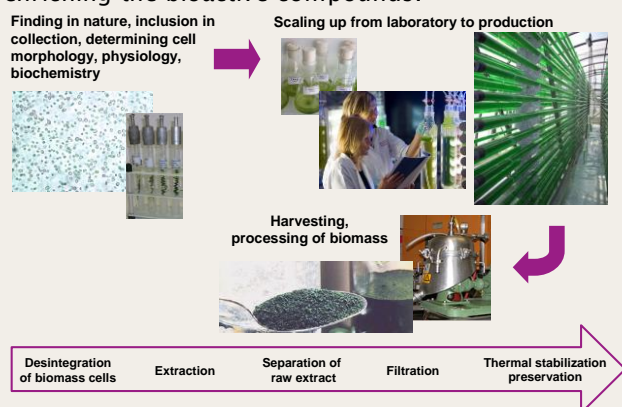


Figure 2: Cyanidium caldarium cultivation and extraction.

TEGO® Stemlastin is COSMOS and NaTrue certified and allows development of sustainable, responsible and natural cosmetic products.

***In vitro* stem cell and fibroblasts studies**

Different *in vitro* studies were carried out to analyze the effects of Cyanidium extract on a biological level. Commercially available epidermal keratinocyte progenitor cells were used as cell culture model to study the effects on epidermal stem cells. Dermal fibroblasts were used to evaluate dermal effects. After treatment of keratinocyte progenitor cells e.g. colony forming efficiency (CFE) was analyzed.

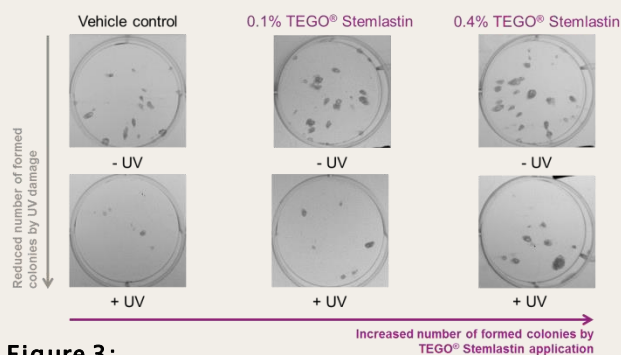
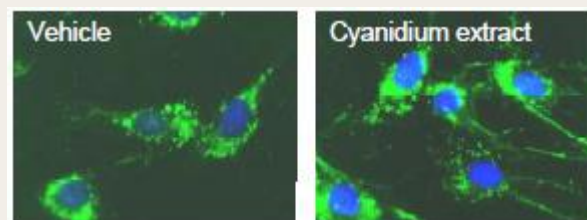


Figure 3: Microscopic pictures of colony forming efficiency (CFE) of epidermal progenitor cells after application of TEGO® Stemlastin with or without UV damage.

The results of this study clearly show that Cyanidium caldarium extract helps the epidermal stem cells to maintain their characteristics, even after damaging the cells with UV light. Therefore, TEGO® Stemlastin will significantly support and protect maintenance of epidermal stem cell activity. In addition, the activity of Cyanidium extract on fibroblasts was evaluated. Among other activities, stimulation of elastin protein production could be observed (not shown).

Hyaluronic acid – affinity histochemistry



Focal adhesions – paxillin staining

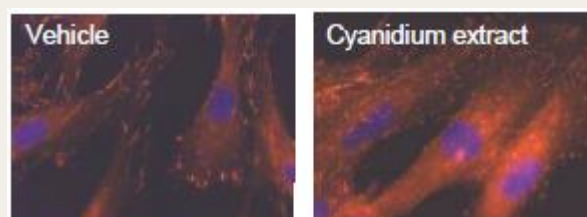


Figure 4: Affinity histochemistry, hyaluronic acid (top) and paxillin (bottom) staining.

Also increased production of HA and general ECM structure support as well as improved interaction of cells with the ECM in the dermal layer could be shown. Therefore, it can be claimed that TEGO® Stemlastin stimulates fibroblast activity leading to more dynamic dermal behaviour.

***In vivo* elasticity study – inner forearm**

Male and female volunteers, aged between 33 and 59 years were recruited for this study, which was conducted in winter time. 19 volunteers received an O/W formulation containing 1% TEGO® Stemlastin, 21 panelists received the formulation containing 5% TEGO® Stemlastin and 20 panelists received the formulation with 2% Malus Domestica extract as a market reference product. 20 Panelists received the formulation without active ingredient (vehicle). Test formulations were applied twice daily for 8 weeks on the inner forearm in a randomized test design. Prior to application and after 8 weeks skin elasticity and

skin surface parameters were determined. Skin elasticity measurements were conducted using a Cutometer MPA 580 (Courage & Khazaka, Cologne, D).

In figure 5 reduction of fine lines is presented after normalization to vehicle. It can be seen that TEGO® Stemlastin improves the skin structure by reducing fine lines after 8 weeks of application compared to the vehicle treatment. These effects can be achieved with 1% TEGO® Stemlastin and they are statistically significant compared to the vehicle formulation when using 5% TEGO® Stemlastin.

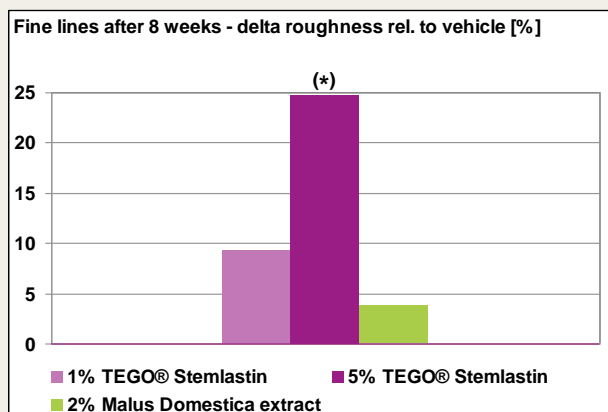


Figure 5: Fine lines expressed as roughness parameters after 8 weeks of application, calculated relative to vehicle treated skin (significance: (*) $p < 0.1$ vs. vehicle).

These effects are in line with an improved skin texture (Figure 6). Skin texture parameters are significantly improved compared to vehicle treatment already with the lower concentration of 1% TEGO® Stemlastin. Using higher concentration does not further improve activity of the extract on skin texture.

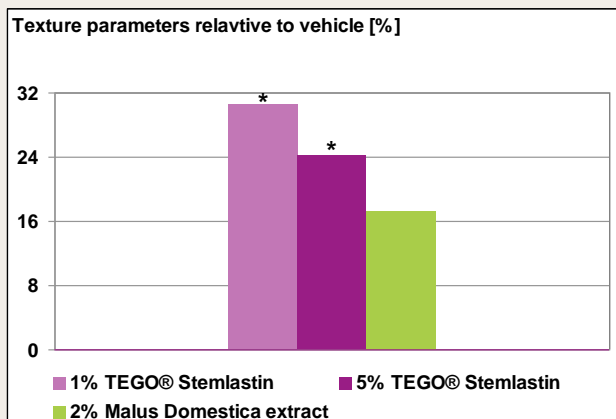


Figure 6: Skin texture parameters after 8 weeks of

application, calculated relative to the vehicle treated skin (significance: * $p < 0.05$ vs. vehicle, ** $p < 0.01$ vs. vehicle). These effects are likely to be due to improved behavior of epidermal progenitor/stem cells. The consequences are improved skin renewal and a smoother and more radiant skin surface. This can be visualized in the images in figure 7. After 8 weeks of treatment with TEGO® Stemlastin, the skin appears to be more even and fine lines are visibly flattened. Malus Domestica extract does not show significant effects with the tested concentration in this study.

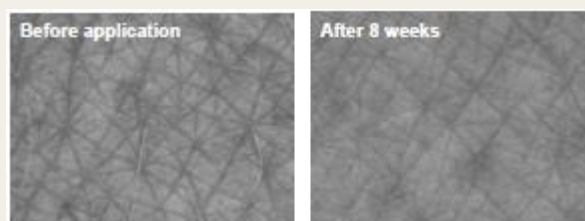


Figure 7: Digital images of the skin surface before and after 8 weeks of application of 5% TEGO® Stemlastin.

Improving skin elasticity requires the active ingredient to “work” in the dermal parts of the skin. To achieve positive effects in the dermis higher concentrations of TEGO® Stemlastin are required. Both skin elasticity parameters that describe the remaining deformation of the skin after stretching are significantly reduced by application of 5% TEGO® Stemlastin compared to vehicle treatment (Figure 8).

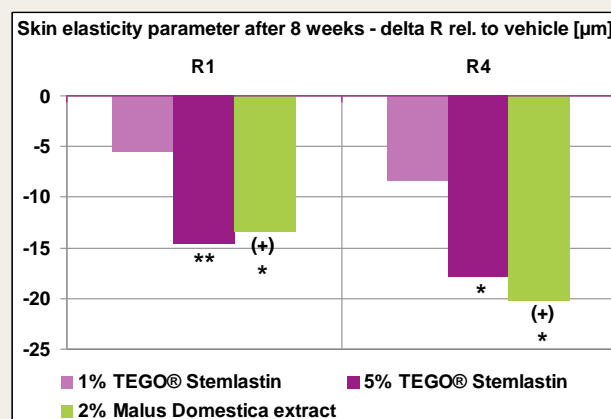


Figure 8: Skin elasticity parameters after 8 weeks of application, calculated relative to vehicle treated skin (significance: + $p < 0.05$ vs. start, * $p < 0.05$ vs. vehicle, ** $p < 0.01$ vs. vehicle).

R1 describes the ability of the skin to bounce back after stretching and R4 describes skin elasticity

fatigue. TEGO® Stemlastin is able to improve both parameters leading to supple skin.

In general, Malus Domestica extract performs in a similar way when it comes to skin elasticity compared to TEGO® Stemlastin. Nevertheless, the cost/performance ratio is much better with TEGO® Stemlastin.

***In vivo* biopsy and anti-wrinkle study – gluteal region and face**

The study was performed at the Institute of Molecular Preventive Medicine (IUF) at the Heinrich Heine University in Duesseldorf, Germany, under the supervision of Prof. Krutmann.

A placebo controlled study enrolling 20 healthy volunteers (female and male) from 50 to 77 years of age was performed in two parts.

For the biopsy part, the volunteers applied once daily in the morning 2 mg/cm² of different O/W test formulations containing either no active ingredient (vehicle), 1% or 5% TEGO® Stemlastin or 0.1% Retinol (anti-aging standard, 0.2% of a commercial 50% Retinol solution were used) on the upper medial quarter of the gluteal region using a randomized test design. After 8 weeks treatment 6 mm punch biopsies were taken from the four different testing areas and gene expression analysis was carried out. The second part of the study was performed on the face. The volunteers applied the O/W formulation without active ingredient on one part of the face and the formulation containing 5% TEGO® Stemlastin on the other side (half-side test design) once daily in the morning for a period of 8 weeks.

Before and after the treatment phase digital images of the face were taken, and image analysis was performed using a VISIA-CR facial imaging system (Canfield Scientific, Inc., NJ, USA). Furthermore, visual expert grading was performed. Dermatologists graded the degree of wrinkle reduction after 8 weeks on a 5 grade scale (1=low wrinkle appearance, 5=high wrinkle appearance) compared to the beginning of the study.

In the first part of this study relative gene expression was analyzed after 8 weeks of application of different test formulations with TEGO® Stemlastin and Retinol compared to the vehicle formulation out of punch biopsies from the gluteal region of the volunteers (Figure 9).

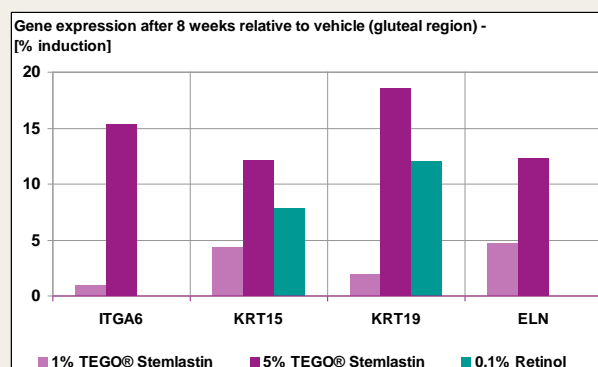


Figure 9: Relative gene expression of α6 integrin, keratin 15, keratin 19 and elastin in punch biopsies of human skin after 8 weeks of treatment with different concentrations of TEGO® Stemlastin and Retinol. Results are calculated relative to the vehicle-treated skin and normalized to 18S rRNA gene expression.

The results show an increased gene expression of relevant stem cell markers at 5% TEGO® Stemlastin pointing out that TEGO® Stemlastin maintains epidermal stem cell characteristics. Furthermore, elastin boosting activity of TEGO® Stemlastin which was already observed in vitro could be confirmed as the elastin gene expression was approximately 2-fold upregulated after 8 weeks application of 5% TEGO® Stemlastin.

In addition, the volunteers applied two test formulations on the face during this study. Wrinkle reduction was analyzed after the application period. Figure 10 shows results from expert grading, where wrinkle formation was evaluated on a 5 grade scale before and after the application of either the vehicle formulation on one side of the face or the formulation with 5% TEGO® Stemlastin on the other side.

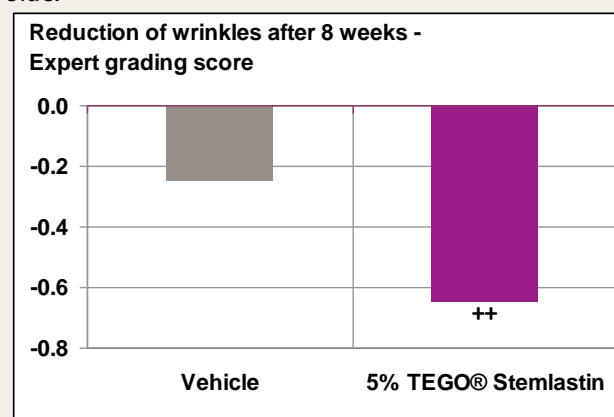


Figure 10: Expert grading of wrinkle formation by treatment with 5% TEGO® Stemlastin or vehicle formulation after 8 weeks (significance: ++p<0.01 vs. start).

The investigation of the experts shows that a significant reduction in the appearance of wrinkles could be observed after 8 weeks treatment with 5% TEGO® Stemlastin.

This is also visible in the image analysis with the VISIA-CR device (Figure 11).



Figure 11: Images of crow-feet before (top) and after (bottom) application of 5% TEGO® Stemlastin for 8 weeks. The right side shows the analysis of the face with the VISIA-CR software. The green lines reflect the wrinkle structures on the face.

The wrinkle reduction after treatment with TEGO® Stemlastin can be seen in the pictures on the left side, and is further illustrated using the VISIA-CR analysis software (right side; green lines reflect wrinkle structures on the face).

Taken together, TEGO® Stemlastin is an innovative active ingredient with broad biological activity, which leads to a youthful appearance and delay of chronological aging.

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

Claim summary

- Protects and maintains epidermal stem cell capacity for rejuvenated skin activity
- Boosts elastic fibers for highly supple skin
- Fights skin elasticity fatigue
- Retains a youthful appearance

Patent position

A patent application describing manufacturing process and cosmetic application of Cyanidium caldarium extract was filed by Evonik Industries AG (WO2013023873A1).

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

Formulation hints

TEGO® Stemlastin is water soluble.

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

The emulsion is prepared as usual. TEGO® Stemlastin is added during the cooling process at temperatures below 40 °C.

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

The emulsion is prepared as usual. TEGO® Stemlastin is added at temperatures below 40 °C. Afterwards the emulsion is cooled to 30 °C and homogenized again.

Recommended usage concentration

Recommended use level 1–5%; clinically tested at different concentrations.

Possible applications

- Anti-aging products which claim on stem cells
- Rejuvenating products for face and body care
- (night cream, serum, mask)
- Natural anti-wrinkle products
- Dual function youth elixir

Packaging

5 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 case of accidents and fires
- toxicity and ecological effects

is given in our material safety data sheets.

Guideline formulations

Power Serum For Aged Skin MM 216/2	
Phase A	
TEGO® Care 450 (Polyglyceryl-3 Methylglucose Distearate)	2.0%
TEGOSOFT® DEC (Diethylhexyl Carbonate)	5.0%
TEGOSOFT® OP (Ethylhexyl Palmitate)	5.0%
TEGOSOFT® OER (Oleyl Erucate)	1.5%
Avocado (Persea Gratissima) Oil	1.5%
Phase B	
TEGO® Pep 4-17 (Tetrapeptide-21; Glycerin; Butylene Glycol; Aqua)	2.0%
HyaCare® 50 (Hydrolyzed Hyaluronic Acid)	0.1%
Glycerin	3.0%
Water	75.9%
Phase C	
TEGO® Carbomer 134 (Carbomer)	0.2%
TEGOSOFT® OP (Ethylhexyl Palmitate)	0.8%
Phase D	
TEGO® Stemlastin (Algae extract)	5.0%
Phase E	
Sodium Hydroxide (10%)	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 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 and E below 40 °C.	
¹⁾ Important: If phase A has to be charged into the vessel first, phase B must be added without stirring	

Natural cell Active Rejuvenation CD 997/3	
Phase A	
TEGO® Care PSC 3 (Polyglyceryl-3 Stearate/Citrate)	3.0%
TEGIN® M Pellets (Glyceryl Stearate)	2.0%
TEGO® Alkanol 18 (Stearyl Alcohol)	1.0%
TEGOSOFT® DO (Decyl Oleate)	10.0%
TEGOSOFT® AC (Isoamyl Cocoate)	5.0%
TEGOSOFT® OER (Oleyl Erucate)	3.0%
Phase B	
Glycerin	3.0%
Water	67.3%
Phase C	
Xanthan Gum	0.5%
Phase D	
TEGO® Stemlastin (Algae extract)	5.0%
Phase E	
Sodium Hydroxide (10% in water)	0.2%
Phase Z	
Preservative, Perfume	q.s.
Preparation:	
1. Heat phase A and B separately to approx. 80 °C.	
2. Add phase A to B with stirring. ¹⁾	
3. Homogenize.	
4. Cool with gentle stirring to approx. 40 °C and add phase C.	
5. Homogenize for a short time.	
6. Cool with gentle stirring and add phase D and E below 40 °C.	
¹⁾ Important: If phase A has to be charged into the vessel first, phase B must be added without stirring	

Youth Intensifying Cream	
CD 997/5	
Phase A	
TEGO® Care PSC 3 (Polyglyceryl-3 Stearate/Citrate)	3.0%
TEGIN® M Pellets (Glyceryl Stearate)	2.0%
TEGO® Alkanol 18 (Stearyl Alcohol)	1.0%
TEGOSOFT® DO (Decyl Oleate)	10.0%
TEGOSOFT® AC (Isoamyl Cocoate)	5.0%
TEGOSOFT® OER (Oleyl Erucate)	3.0%
Phase B	
Glycerin	3.0%
Water	69.0%
Phase C	
Xanthan Gum	0.5%
Phase D	
TEGO® Stemlastin (Algae extract)	3.0%
Phase E	
Sodium Hydroxide (10% in water)	0.2%
Phase Z	
Preservative, Perfume	q.s.
Preparation:	
1. Heat phase A and B separately to approx. 80 °C.	
2. Add phase A to B with stirring. ¹⁾	
3. Homogenize.	
4. Cool with gentle stirring to approx. 40 °C and add phase C.	
5. Homogenize for a short time.	
6. Cool with gentle stirring and add phase D and E below 40 °C.	
¹⁾ Important: If phase A has to be charged into the vessel first, phase B must be added without stirring	

Especially concerning Active Ingredients

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