TEGO® Pep 4-Even

Balancing skin tone

- A peptide sequence derived from the skin's own structure
- Active on all kinds of skin types
- Visibly diminishes hyperchromatic spots
- Brightens skin and improves the evenness of skin tone
- Reduces acne lesions
- Alleviates melasma on ethnic skin
- Provides a significant anti-inflammatory effect
- Safely inhibits the pigmentation process and is skin-friendly
- Preservative-free peptide solution
- Patent-protected application by Evonik
- Shows good stability in formulation and is compatible with sunscreens
- Usage concentration: 0.5 - 5.0 %

Personal Care

INCI Name (PCPC name)
Tetrapeptide-30; Glycerin

Chemical and physical properties (not part of specifications)	
Form	colorless, clear liquid
Active matter	approx. 1600 ppm

TEGO® Pep 4-Even is a preservative-free solution of Tetrapeptide-30 (Amino acid sequence Proline – Lysine – Glutamic Acid – Lysine; PKEK) in glycerin and water.

Properties

Skin tone and its evenness are very important cosmetic issues all over the world. While people in Asia want to get a lighter overall skin tone, people in Europe focus more on the reduction of hyper-chromatic spots (age spots). People with ethnic skin, on the other hand, often suffer from an irregular skin appearance (mottled hyperpigmentation), so their main intention is the improvement of the evenness of skin tone.

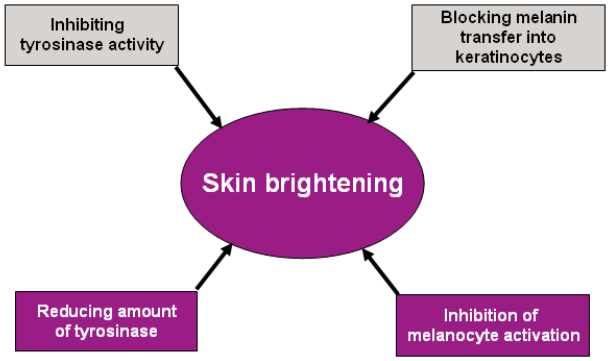


Figure 1: Factors involved in skin tone modulation

TEGO® Pep 4-Even contributes to an even skin tone. This is achieved via an anti-inflammatory activity of the peptide that finally leads to a reduction of the amount of tyrosinase and an inhibition of melanocyte activation.

To obtain optimal results for skin brightening, most cosmetic formulations combine two or more active ingredients that address additional factors involved in skin tone modulation, like a tyrosinase inhibitor or a substance reducing the melanin transfer.

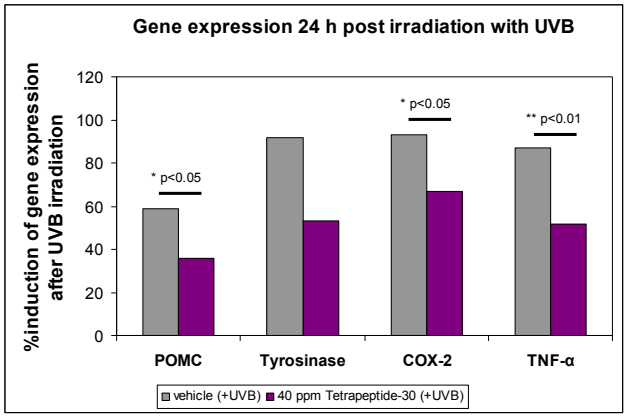
***In vivo* study overview conducted for claim support:**

Test	Number of panelists	Measurement	Results
Biopsy study	10	RT-PCR of melanogenic and inflammation markers after UV-irradiation	Reduction of POMC, Tyrosinase, COX2, TNF-α, IL-6, IL-8
Skin lightening study, hand	38	Skin color (Colorimeter) Digital images	Skin brightening & reduction of erythema
Anti-age spot study on Caucasian skin, face	40	Skin color (Chromameter) Digital images	Reduction of age-spots & increased activity by combining with Sodium Ascorbyl Phosphate
Study on Asian skin, face	27	Skin color (Colorimeter) Controlled digital photographs	Reduction of uneven skin tone & brightening of the skin
Study on ethnic skin, face	50	Controlled digital photographs Clinical assessment (expert grading)	Improvement of skin evenness by reduction of melasma and acne lesions

Concentration of pure Tetrapeptide-30 in all studies: 40 ppm (or 2.5 % of TEGO® Pep 4-Even)

- ***In vivo* biopsy study: Reduction of melanogenesis activation in human skin**

An *in vivo* biopsy study was performed, in order to prove the mitigating effect of Tetrapeptide-30 on keratinocyte-secreted factors that are involved in melanocyte activation via anti-inflammatory mechanisms.



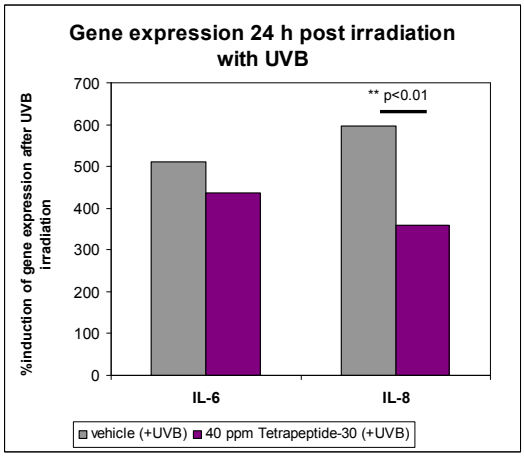


Figure 2: Induction of gene expression of POMC, Tyrosinase and different inflammation markers in punch biopsies of human skin after 4 weeks

Following four weeks of treatment with Tetrapeptide-30, the skin was exposed to 1.5 MED of UV irradiation. This reduced the gene expression of the melanogenic and inflammation markers. This confirms the smart skin brightening mechanism of TEGO® Pep 4-Even, which shows anti-inflammatory activity by influencing cell-cell communication between keratinocytes and melanocytes

- ***In vivo*** **efficacy study on Caucasian skin: Lightening the skin tone on the hand**

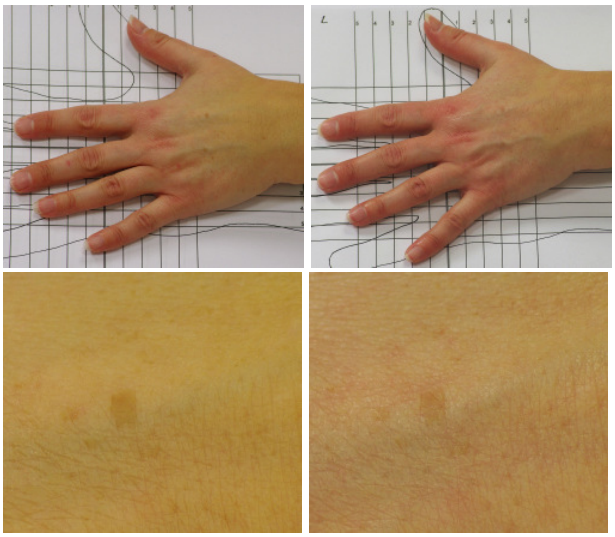


Figure 4: Reduction of yellowish skin color and age spots on the hand by Tetrapeptide-30 in combination with Sodium Ascorbyl Phosphate (left side: start, right side: after 8 weeks)

To evaluate the performance of Tetrapeptide-30, the study was performed against a vehicle containing a Vitamin C derivative (Sodium Ascorbyl Phosphate), a well-known tyrosinase inhibitor. The results underlined that Tetrapeptide-30 has a skin brightening activity that is accompanied by a reduction of skin redness, verifying the anti-inflammatory activity of the peptide. Additionally, a strong fading of hyperchromatic age spots of the skin was observed.

- ***In vivo efficacy*** **study on Caucasian skin: Reduction of facial age spots**

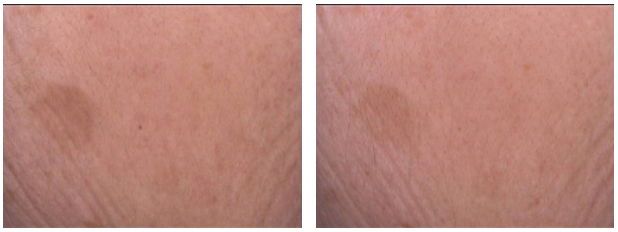


Figure 5: Reduction of facial age spots by Tetrapeptide-30 in combination with Sodium Ascorbyl Phosphate (left side: start, right side: after 6 weeks)

Tetrapeptide-30 led to a visible fading of the hyperchromatic spots which make it an interesting choice for anti-aging products. In combination with Sodium Ascorbyl Phosphate, the efficacy of the cosmetic formulations was further optimized.

- ***In vivo*** **efficacy study on Asian skin: Improvement of evenness of skin tone**

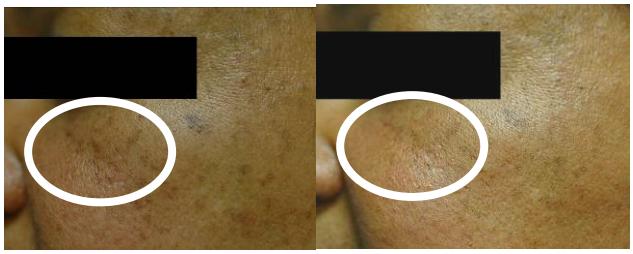


Figure 6: Panelist with reduced hyperpigmentation by Tetrapeptide-30 in combination with Sodium Ascorbyl Phosphate (left side: start, right side: after 8 weeks)

Over the period of the study no change in hyperpigmentation was observed for the vehicle-group (only Sodium Ascorbyl Phosphate) whereas the combination of SAP with Tetrapeptide-30 showed a reduction in hyperpigmentation of about 15 %. This demonstrated that Tetrapeptide-30 is able to reduce the major concerns of Asian skin: it lightens the skin and improves the evenness of skin tone.

- ***In vivo*** **efficacy study on ethnic skin: Improvement of evenness of skin tone**

Figure 7: Panelist with reduced number of acne lesions (left side: start, right side: after 12 weeks)

The study results revealed that Tetrapeptide-30 is also able to reduce the major disorders of ethnic skin: it improves the evenness and the overall appearance of skin. Additionally, it reduces the number of lesions caused by acne.

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

Claim Summary

TEGO® Pep 4-Even

- is active on all kinds of skin types
- has a smart skin tone brightening mechanism
- improves the evenness of skin tone
- brightens skin
- visibly diminishes hyperchromatic spots
- provides a significant anti-inflammatory effect
- reduces acne lesions
- alleviates melasma on ethnic skin

Patent position

The use of TEGO® Pep 4-Even (Sequence "PKEK") in cosmetic formulations is subject of patent application WO 2009068351.
A second, yet undisclosed, application claiming the use of PKEK for certain cosmetic use has been filed by Evonik Goldschmidt GmbH in November 2009.

Helix Biomedix is the applicant and owner of PCT application WO2008085494 claiming short bioactive peptides for cellular and immunological modulation. Evonik Goldschmidt GmbH and Helix Biomedix have entered into a licensing agreement in August 2007 assuring Evonik Goldschmidt GmbH exclusive rights to market peptides under said IP worldwide.

To the best of our knowledge, no third party patent right exists that generally prevents customers from using TEGO® Pep 4-Even in cosmetic formulations.

Formulation hints

TEGO® Pep 4-Even is a water soluble, easy to formulate peptide solution.
For the preparation of any kind of cosmetic formulation, TEGO® Pep 4-Even is simply added to the water phase and the emulsion (O/W or W/O) is prepared as usual. For O/W emulsions, it is also possible to add TEGO® Pep 4-Even during the cooling process.

Store at 4 – 8 °C.

Recommended usage concentration

Recommended use level 0.5 % – 5.0 %;
clinically tested at 2.5 %.

Applications

- Skin lightening preparations
- Anti-aging preparations with correction of age spots & pigmentation disorders
- Anti-aging products for even skin tone
- Ethnic skin care
- Hand creams
- Décolletté preparations

Packaging

1.0 kg package

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 sheet.

Guide Line Formulations

Balancing Skin Tone Hand Cream, SPF 15 1/3 UVA CL 15/10-2	
Phase A	
TEGO® Care PSC 3 (Polyglyceryl-3 Dicitrate/Stearate)	3.00 %
TEGO® Alkanol 1618 (Cetearyl Alcohol)	1.25 %
TEGIN® M Pellets (Glyceryl Stearate)	1.25 %
TEGOSOFT® DEC (Diethylhexyl Carbonate)	2.50 %
TEGOSOFT® OER (Oleyl Erucate)	2.00 %
TEGOSOFT® MM (Myristyl Myristate)	1.20 %
TEGOSOFT® CT (Caprylic/Capric Triglyceride)	3.00 %
Bis-Ethylhexyloxyphenol Methoxyphenyl Triazine (TINOSORB S, BASF SE)	3.00 %
Octocrylene	3.50 %
TEGO® Sun TDEC 45 (Titanium Dioxide; Diethylhexyl Carbonate; Polyglyceryl-6 Polyhydroxystearate)	4.40 %
Phase B	
Glycerin	3.00 %
Water	66.65 %
Phase C	
TEGO® Pep 4-Even	2.50 %
Phase D	
TEGO® Carbomer 134 (Carbomer)	0.15 %
TEGOSOFT® DC (Decyl Cocoate)	1.00 %
Xanthan Gum	0.20 %
Phase Z	
Sodium Hydroxide (10 % in water)	0.40 %
Phenoxyethanol; Ethylhexylglycerin (EUXYL PE 9010, Schülke & Mayr GmbH)	1.00 %
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. Homogenise.
4. Cool with gentle stirring to approx. 50 °C and add phase C and D.
5. Homogenise for a short time.
6. Cool with gentle stirring and add phase Z below 40 °C. Adjust pH to 6-7.

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

Correcting Moisturizer for Even Skin CD 935/1	
Phase A	
AXOL® C 62 Pellets (Glyceryl Stearate Citrate)	1.5 %
TEGO® Alkanol 1618 (Cetearyl Alcohol)	3.0 %
TEGIN® M Pellets (Glyceryl Stearate)	1.0 %
TEGOSOFT® liquid (Cetearyl Ethylhexanoate)	11.0 %
TEGOSOFT® OP (Ethylhexyl Palmitate)	11.0 %
TEGOSOFT® MM (Myristyl Myristate)	2.0 %
Phase B	
Glycerin	5.0 %
Water	47.9 %
Phase C	
TEGO® Carbomer 134 (Carbomer)	0.2 %
TEGOSOFT® OP (Ethylhexyl Palmitate)	0.8 %
Phase D	
TEGO® Pep 4-Even	2.5 %
Sodium Ascorbyl Phosphate	1.5 %
Urea	2.5 %
Sodium Bisulfite	0.1 %
Water	10.0 %
Phase E	
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. Homogenise.
4. Cool with gentle stirring to approx. 50 °C and add phase C.
5. Homogenise for a short time.
6. Cool with gentle stirring and add phase D and E below 40 °C. Adjust pH to 7.

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

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