FGF2-STAB® Polypeptide

Stabilized Fibroblast Growth Factor 2

Anti-aging ingredient with **increased stability** when compared to the native form of FGF2 protein

- Retains skin hydration
- Reduces wrinkles
- Enables skin softening
- Normalizes skin keratinization

Suitable for aging skin, dehydrated skin, skin with wrinkles and uneven textured skin.

FIBROBLAST GROWTH FACTOR 2 (FGF2)

Fibroblast Growth Factor 2 (FGF2) is one of the most versatile human growth factors and an important signalling molecule for many cellular processes. It is involved in the regulation of proliferation, differentiation, and migration of various cell types. In addition to its essential role during embryogenesis and tissue development, FGF2 is involved in the healing processes of damaged tissues [1]. Several preclinical [2-4] and clinical [5-7] studies have shown that FGF2 has a positive effect on the healing of poorly healing (chronic) wounds, such as diabetic foot syndrome, pressure ulcers, burns, or postoperative wounds. These studies specifically demonstrated that FGF2 promotes fibroblast migration, collagen maturation, supports the formation of new blood vessels (angiogenesis), and tissue re-epithelialization (Figure 1). Further studies have shown that FGF2 increases skin elasticity, reduces wrinkle depth, enhances skin hydration, reduces pigmentation levels, and promotes hair growth by inducing the anagen phase of hair follicles [8-10].

At the molecular level, FGF2 functions as a signalling molecule by binding to the fibroblast receptor (FGFR). Signal transduction occurs on the outer surface of the cell, where a complex is formed consisting of two FGF2 molecules, two FGFR receptors, and one heparan sulphate molecule (HSPG) acting as a cofactor for FGF2 [11]. As a result, structural changes in FGFR receptors occur, accompanied by the phosphorylation of their kinase domains and subsequent signal transduction to downstream pathways such as the RAS-MAPK cascade (cell growth and differentiation), the PI3K-AKT pathway (cell cycle regulation), the PLCy pathway (cell proliferation, migration, and apoptosis), the Wnt-β-catenin pathway (angiogenesis), and the STAT pathway (embryogenesis, cell division) [12].

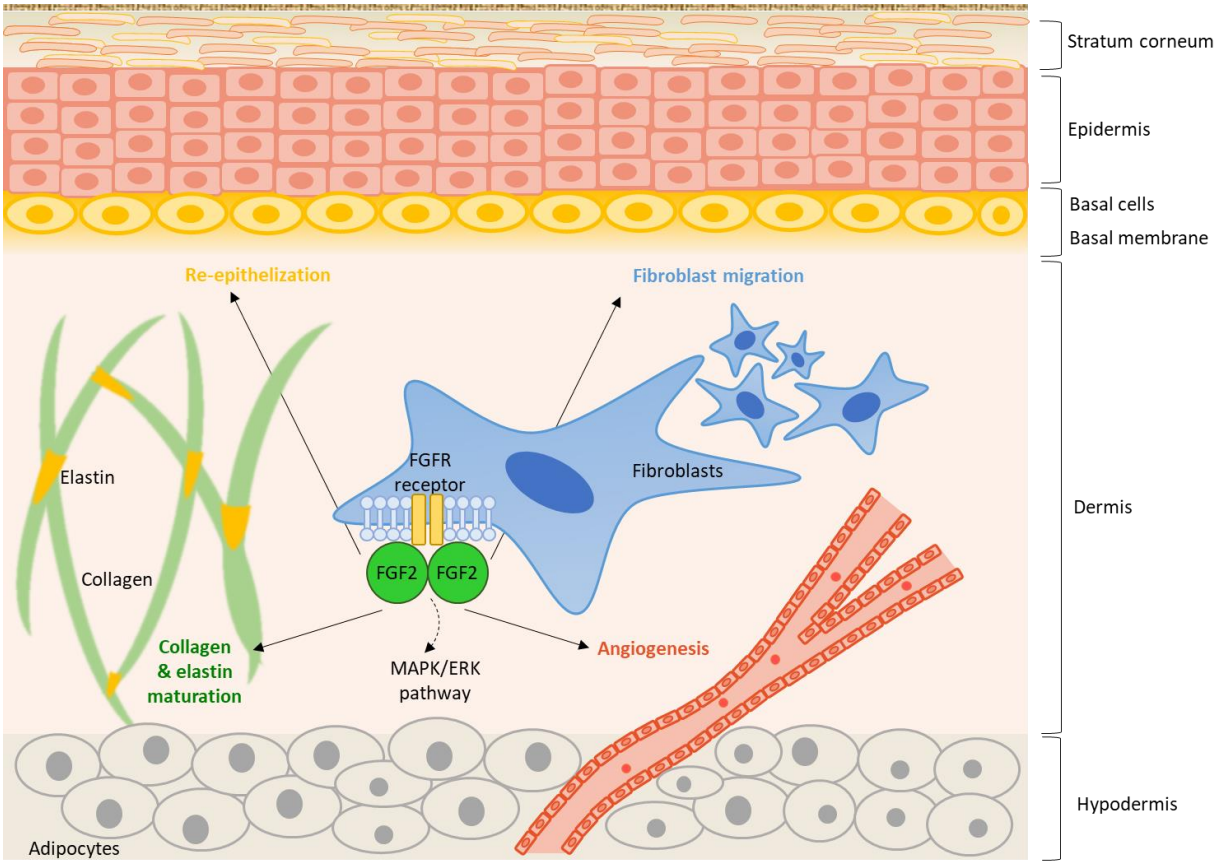


Figure 1 *The mechanism of action of FGF2 in human cells involves the binding of FGF2 as a dimer to the fibroblast receptor (FGFR). Subsequently, structural changes occur in the receptor, leading to the transduction of signals to downstream cellular pathways and cascades.*

FGF2-STAB®

Fibroblast growth factors, including wild-type FGF2, are inherently unstable, which significantly limits their use in industry, medicine, and cosmetics. However, Enantis has developed a stabilized form of FGF2 called FGF2-STAB®, which is more than 50 times more stable than FGF2. Through protein engineering methods, 9 amino acids of the FGF2 protein chain have been substituted, resulting in a 20°C increase in the protein's melting temperature. The higher melting temperature of FGF2-STAB® extends the stability to more than 14 months at room temperature, while the concentration of native FGF2 reduces to 30 % in two weeks) [13,14]. The stabilization of FGF2-STAB® is achieved directly within the protein structure without the use of additional stabilizing agents while preserving the same biological activity (Figure 2). FGF2-STAB® brings economic benefits to cosmetics manufacturers due to significantly slower degradation during production, storage, transportation, and after package opening. The higher stability of FGF2-STAB® also allows the preparation of final cosmetic formulations with a reduced amount of stabilizing agents, reducing the risk of undesired (allergic) reactions.

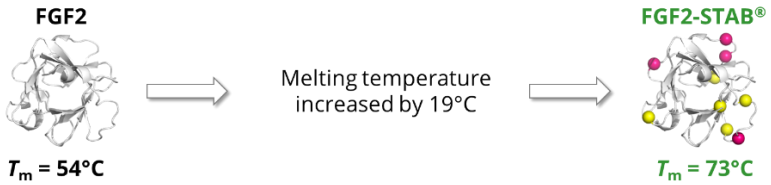


Figure 2 *Stabilization of FGF2 through protein engineering methods involved the substitution of a total of 9 amino acids in the FGF2 protein sequence with others that increase the protein's melting temperature and, consequently, its overall stability.*

Application

Due to the worldwide aging population, there is an increasing interest in regenerative cosmetics. The use of FGF2-STAB® in skincare involves rejuvenating epidermal cells and fibroblast cells, which are responsible for the production of collagen, elastin, and hyaluronic acid. With age, the synthesis of collagen, elastin, and hyaluronic acid slows down and eventually comes to a halt [15]. Instead of undergoing procedures involving the use of botulinum toxin or hyaluronic acid injections, wrinkle minimization and prevention can be achieved through the application of FGF2-STAB®. Maintaining labile FGF2 in cosmetic products active is nearly impossible, and that is why the highly stable growth factor in the form of FGF2-STAB® represents a revolutionary cosmetic ingredient.

FGF2-STAB® SPECIFICATION

TYPE:	Human recombinant protein
INCI:	SH-POLYPEPTIDE-1
CAS NUMBER:	106096-93-9
SOURCE	Bacteria *Escherichia coli* BL21 (DE3)
FERMENTATION MEDIA	Glycerol, $(NH_4)_2HPO_4$, KH_2PO_4, citric acid, $MgSO_4.7H_2O$, Fe(III) citrate, $Na_2MoO_4.2H_2O$, $CoCl_2.6H_2O$, $MnCl_2.4H_2O$, $CuCl_2.2H_2O$, H_3BO3, $Zn(CH_3COOH)_2.2H_2O$
APPEARANCE:	White crystalline powder
BUFFER:	250 mM NaCl, 16.4 mM K_2HPO_4, 3.6 mM KH_2PO_4, pH 7.5
PURITY:	>95% by SDS PAGE (reduced conditions)
MOLECULAR WEIGHT:	19.5 kDa
NUMBER OF AMINO ACIDS:	175
AMINO ACIDS:	Ala – 11 x (6.3 %), Arg – 11 x (6.3 %), Asn – 6 x (3.4 %), Asp – 8 x (4.6 %), Cys – 3 x (1.7 %), Gln – 4 x (2.3 %), Glu – 8 x (4.6 %), Gly – 19 x (10.9 %), His – 9 x (5.1 %), Ile – 6 x (3.4 %), Leu – 15 x (8.6 %), Lys – 14 x (8.0 %), Met – 4 x (2.3 %), Phe – 9 x (5.1 %), Pro – 11 x (6.3 %), Ser – 14 x (8.0 %), Thr – 7 x (4.0 %), Trp – 1 x (0.6 %), Tyr – 8 x (4.6 %), Val – 7 x (4.0 %), Pyl – 0 x (0.0 %), Sec – 0 x (0.0 %)
ISOELECTRIC POINT:	9.54
PH RANGE:	5.5-7.5
ENDOTOXINS:	Endotoxin levels <0.1 ng/µg protein (<1 EU/µg) by LAL test
BIOLOGICAL ACTIVITY:	ED_{50} <1.1 ng/ml, cell proliferation assay using NIH/3T3 mice fibroblasts
PROTEIN CONCENTRATION:	Detected by UV spectroscopy (Protein A280, NanoDrop Spectrophotometers)

Production scheme

FGF2-STAB® is a recombinant protein produced in bacterial *E. coli* strain - BL21 (DE3) by microbial fermentation. All genetic material from the bacteria is removed upon purification process and FGF2-STAB® comes as an animal-free lyophilized powder. Salts in the final powder formulation have mineral origin from mines (NaCl) or mineral-derived origin (K_2HPO_4 and KH_2PO_4)

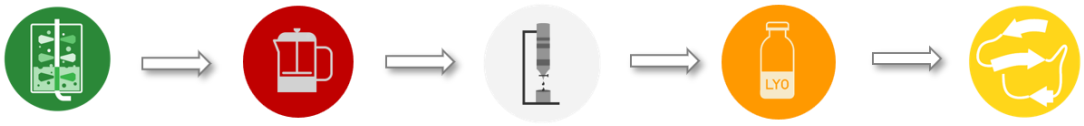


Figure 3 Production pipeline of FGF2-STAB® recombinant protein. Fermentation is done in an animal free, non-GMO Luria Bertani media and quality control is proved by the Certificate of Analysis (CoA).

Dosing

FGF2-STAB® can be used in cosmetic formulations such as creams, gels, serums, etc. The recommended concentration of FGF2-STAB® to achieve the desired effect is **10 µg/ml in the final formulation (10 ppm, 0.001 %)**.

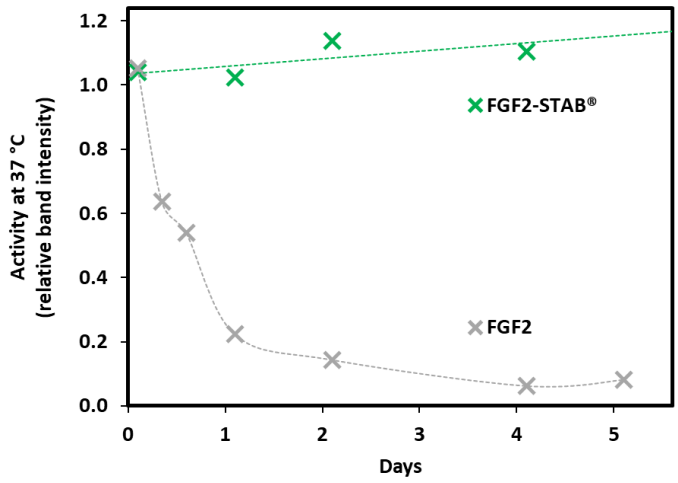
Shelf-life

FORMULATION	TEMPERATURE	SHELF LIFE
Lyophilized	Room temperature to -20 °C	3 years
Reconstituted in water	4 °C	2 years
Reconstituted in water	Room temperature	14 months[i]

FGF2-STAB® vs FGF2 comparison in aqueous solution

	FGF2	FGF2-STAB®	FGF2-STAB® BENEFITS
ACTIVITY AT 37 °C	< 10 hours	> 20 days	More stable during biological processes
STABILITY AT 25 °C	< 1 month	> 14 months[i]	Stable for a longer period (transport and storage)
ACTIVITY (ED_{50})	5.0 ng/ml	1.1 ng/ml	Lower concentration required (reduced costs)
MELTING TEMP.	54 °C	73 °C	Stable at higher temp. (heating during production)

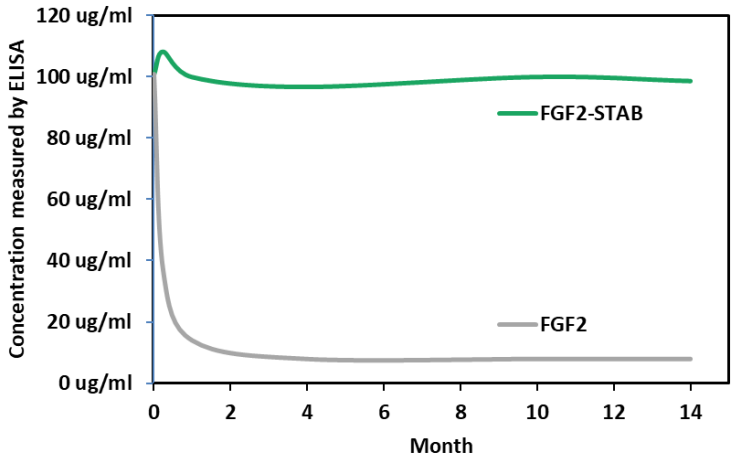
Retained biological activity in solution at 37 °C



The resistance of FGF2-STAB® to higher temperatures results in a significantly longer half-life compared to unstable FGF2. While the biological activity of native FGF2 decreases over time with thermal preincubation, even after just a few hours, the stabilized variant FGF2-STAB® maintains complete biological activity during the 20-day time-course (the later time points are not showed) [13,14]. Experimental data were obtained through quantitative detection of the phosphorylated form of the ERK-1/2 downstream signalling pathway, which is regulated by FGF2. Quantification was performed using the western blotting from the lysate of CCTL14 embryonic stem cells.

[i] Ongoing long-term stability testing up to 2 years

Long-term stability in aqueous solution at 25 °C



Concentration of native FGF2 drops to less than 50 % in 1 week at room temperature, limiting its utilisation in cosmetics industry. Concentration of FGF2-STAB® is stable for several months (ongoing long term stability experiment). Concentration was detected by ELISA using specific antibody recognizing FGF2-STAB®.

Heavy metals content

FGF2-STAB® Cosmetics ingredient complies with the EU Cosmetics Regulation (EC No 1223/2009) and **does not exceed** the specified heavy metals limits.

Element		**FGF2 STAB®**	**Limit***
Lead	Pb	0.002212 ppm	2 ppm
Cadmium	Cd	0.000143 ppm	0.1 ppm
Nickel	Ni	0.025220 ppm	10 ppm
Arsenic	As	0.035480 ppm	0.5 ppm
Mercury	Hg	Not detected	0.1 ppm
Antimony	Sb	Not detected	0.5 ppm
Chromium	Cr	Not detected	1 ppm

The presence of heavy metals in FGF2-STAB® Cosmetics was determined by ICP/MS in the *Laboratory of atomic spectrochemistry, Masaryk University, Brno, Czech Republic*.

** Limits for final cosmetic products*

ISO 16128 Natural origin index calculation

Based on the ISO 16128-1:2016 (Definitions for ingredients) and ISO 16128-2:2017 (Criteria for ingredients and products), FGF2-STAB® **is composed of natural origin components** and FGF2-STAB® has **Natural Origin Index (NOI) = 1** and therefore it is compliant with ISO 16128.

Component	**Origin**	**Molecular weight**	**Weight per 1 l**
1 mg/ml FGF2-STAB®	Fermentation	19497.20 g/mol	1 g
250 mM NaCl	Mineral	58.44 g/mol	14.61 g
16.4 mM K_2HPO_4	Mineral	174.18 g/mol	2.855 g
3.6 mM KH_2PO_4	Mineral	136.09 g/mol	0.490 g
Total			***18.955 g***

$$NOI = \left(\frac{weight\ of\ natural\ ingredients}{total\ weight\ of\ solution}\right) x100$$

$$NOI = \left(\frac{1\ \text{g (FGF2-STAB®)} + 14.61\ \text{g (NaCl)} + 2.855\ \text{g } (K_2HPO_4) + 0.490\ \text{g } (KH_2PO_4)}{18.955}\right) x100$$

$$NOI = \left(\frac{18.955}{18.955}\right) x100 = \mathbf{100\ \%}$$

In vivo EFFICACY RESULTS

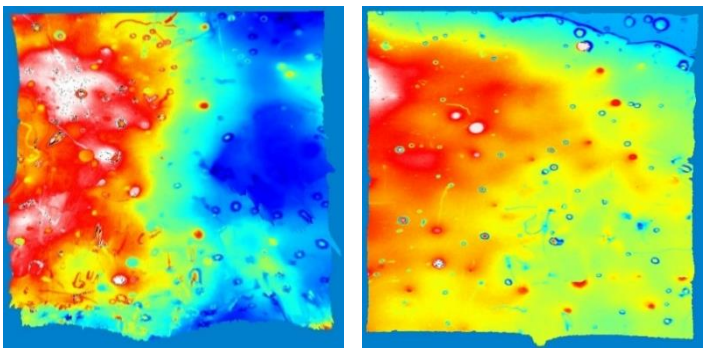
FGF2-STAB® reduces wrinkles and lowers the skin roughness

Improved skin aesthetics

The application of FGF2-STAB® in a cream formulation for a period of 2 months resulted in a visible reduction of wrinkles and a decrease in skin roughness. Images capture the changes in a representative individual.

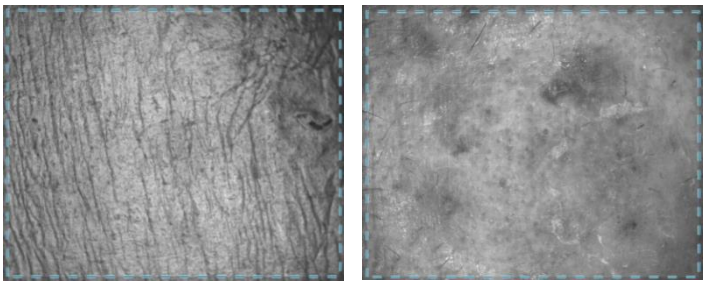
Skin surface normalization

The use of FGF2-STAB® cream resulted in the smoothing of the skin texture, as captured by the Visiometer device. The improvement in skin surface evenness directly correlates with the reduction of irregularities, including wrinkles. The red colour represents deeper areas, while the blue colour represents higher areas of the skin profile. Application of FGF2-STAB® reduced differences between minimums and maximums of the skin profile. Images capture the changes in a representative individual.

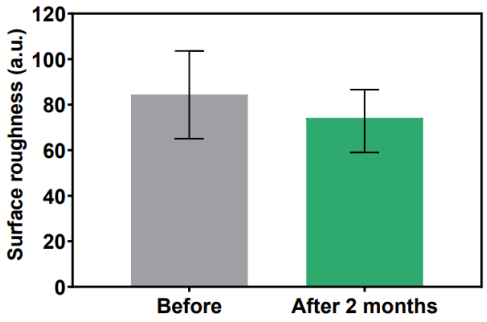


Lower skin roughness

The product containing FGF2-STAB® also reduced the average roughness of the skin surface, as measured by the Visioscan device (images capture the changes in a representative individual).

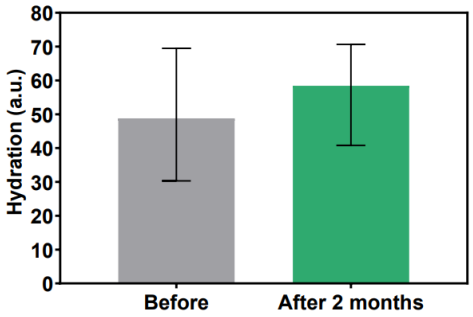


In over 50 % of the subjects, a decrease in the roughness parameter was observed (see the graph).



Increased skin hydration

FGF2-STAB® in the cream formulation increased the hydration of the stratum corneum in over 50% of the individuals tested. The assessment of hydration was based on the measurement of dielectric capacitance of the outer layers of the skin. This method eliminates the disadvantages of assessing hydration based on conductivity/resistance but is significantly less sensitive to sweating factors.



Design of *in vivo* evaluation

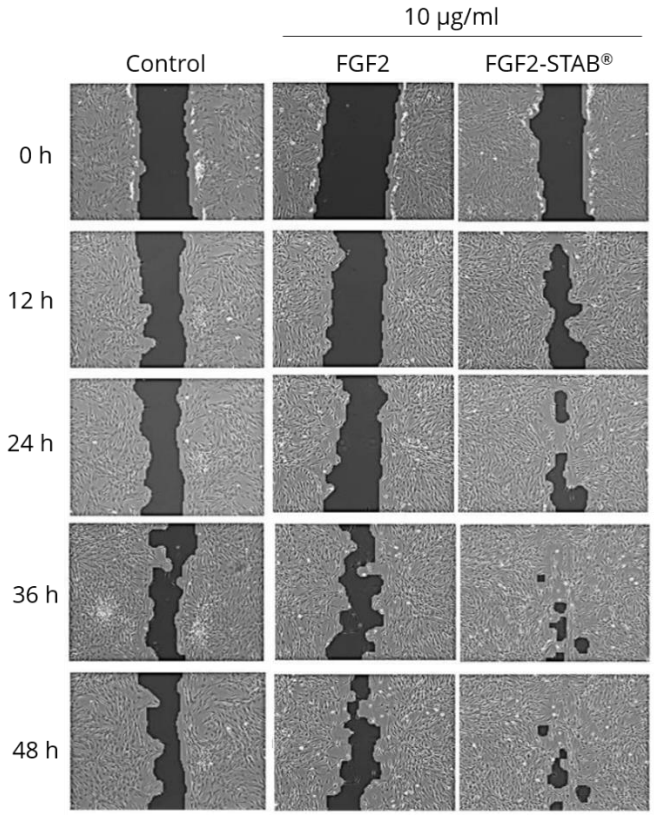
The *in vivo* evaluation was conducted by Syncare Plus on 19 volunteers. To demonstrate the effect of FGF2-STAB, the simplest cream formulation without components that could potentially overshadow the measured parameters was used. The composition of the cream for in vivo testing included Aqua, Oenothera Biennis Oil, Glycine Soya, Cymbopogon Citratus leaf oil, Glycerin, Pentylene Glycol, Urea, Cetyl Alcohol, Methyl Glucose Sesquistearate, FGF2 STAB®, Sodium Hyaluronate, Butyrospermum parkii butter, Ethylhexylglycerin, Sesamum Indicum seed oil, Citrus Aurantium dulcis oil, Lavandula Angustifolia flower oil, Rosmarinus Officinalis Leaf Extract, Alcohol denat., Phenoxyethanol, Limonene, Geraniol, Linallol. The study was performed from December 15, 2022, to February 24, 2023, under the supervision of the Syncare Plus Center for Aesthetic Dermatology, meeting the requirements of Article 20 of Regulation 1223/2009/EC. The trial was methodically conducted in accordance with ČSN EN ISO 14155 - Clinical investigation of medical devices for human subjects, with the approval of the Ethics Committee of Syncare Plus s.r.o.

In vitro EFFICACY RESULTS

Increased re-epithelization of human fibroblasts

FGF2-STAB® promotes tissue re-epithelization in a shorter period of time (higher efficiency) compared to FGF2 in the human dermal fibroblast scratch test.

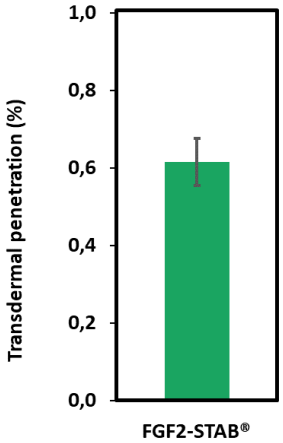
Normal human dermal fibroblasts were isolated from facial skin removed during cosmetic plastic surgery with the informed agreement of the donors. Cells were cultured to confluence and serum-starved for 24 h. After starvation, the scratch was induced by pipette tip and the cells were treated with 10 µg/ml FGF2 and FGF2-STAB® respectively. Pictures of the migrating cells were taken by a microscope and analyzed by TScratch software to determine the reduction of the scratched areas and monitor the cell migration.



Effective transdermal penetration

FGF2-STAB® is capable of skin penetration with relatively high efficacy in comparison to similar molecules with high molecular weight.

Penetration efficacy was determined using a STRAT-M membrane in Franz cells for 24 h and FGF2-STAB® was detected with a specific antibody using ELISA (n=5).



EU COMPLIANCE

EU Regulation No. 1223/2009

FGF2-STAB® **is compliant** with EU Regulation No. 1223/2009, including technical documentation, safety information and MSDS.

FGF2-STAB® (INCI: SH-POLYPEPTIDE-1) **is not** listed as a restricted substance in Annex III of EU Regulation No. 1223/2009

EU Allergens

In compliance with **EU Regulation No 1169/2011**, FGF2-STAB® **does not** contain any allergens listed in Annex II.

Annex II Allergens:

- Cereals containing gluten: namely wheat (including specific varieties like spelt and Khorasan), rye, barley, oats and their hybridised strains) and products thereof
- Crustaceans and products thereof (for example prawns, lobster, crabs and crayfish)
- Egg and products thereof
- Fish and products thereof
- Peanut and products thereof
- Soybeans and products thereof
- Milk and products thereof (including lactose)
- Nuts: namely almond, hazelnut, walnut, cashew, pecan nut, Brazil nut, pistachio nut and Macadamia nut (Queensland nut) and products thereof
- Celery and products thereof
- Mustard and products thereof
- Sesame seeds and products thereof
- Sulphur dioxide and sulphites (at concentrations of more than 10mg/kg or 10mg/L in terms of the total SO2 which are to be calculated for products as proposed ready for consumption or as reconstituted according to the instructions of the manufacturers)
- Lupin and products thereof
- Molluscs and products thereof (for example clams, oysters, scallops, snails and squid)

SAFETY DATA

In vitro cytotoxicity

The toxicological profile of FGF2-STAB® was assessed through *in vitro* testing using the MTT cytotoxicity assay (VERO CCL-81 kidney fibroblast cell line, African green monkey. In accordance with the standards specified in ČSN EN ISO 10993-5, it was demonstrated that the **FGF2-STAB at a concentration of 1500 µg/ml did not exhibit cytotoxic potential under the chosen test conditions**. The complete test protocol is available upon request.

Irritation of FGF2-STAB® cream

Dermatologically tested = Yes

Primary skin irritation test = In 1 out of 20 tested individuals aged 18 to 65, a barely noticeable erythema (mild irritation) without any allergic sensitization reaction was observed => the product demonstrates good skin tolerance.

Sensitivity/Hypoallergenicity according to Human Repeated Insult Patch Test = no sensitive reactions were observed in all 20 tested individuals aged 18 to 65 => the product can be classified as hypoallergenic.

In vivo tests

No observed adverse effect (NOAEL) = 100 µg/kg/day (dogs, intravenously, 28 days) [16]

Safety evaluation in FGF2-STAB® cream

Expected skin exposure area = 965 cm^2 [17]
Daily exposure dose = 1 600 mg (applied twice daily - 0.8 g each time)
Body weight of the individual = 60 kg [17]
Relative daily exposition ($E_{product}$)= 26.7 mg/kg body weight/day

$$\left(E_{product} = \frac{daily\ exposition\ dose}{human\ body\ weight} = \frac{1600}{60}\right)$$

Dermal absorption (DAp) = 0.6% (transdermal penetration of FGF2-STAB through the STRAT-M membrane)
Substances > 500 Da = very low dermal absorption => DAp ≈ 50% [17]
Recommended concentration of FGF2-STAB® in the cosmetic product = 10 µg/ml (final concentration)
Retention factor according to the product type (face cream) = 1 [17]

The systemic exposure dose (SED) considering the 0.6% dermal absorption is calculated as 0.0000016 mg/kg body weight/day.

$$\left(SED = E_{product}\ x \frac{C}{100} x \frac{DA_p}{100} x\ f_{ret} = 26.7\ x \frac{0.001}{100} x \frac{0,6}{100} x\ 1\right)$$

The systemic exposure dose (SED) considering the 50% dermal absorption is calculated as 0.00013 mg/kg body weight/day.

The Margin of Safety (MoS) when considering a 0.6% dermal absorption and utilizing the dose with no apparent toxic effect, extra default value (50%) due to no oral bioavailability data and default factor 3 (no 90-day study, but only 28-day) in the calculation is 1 041. $\left(MoS = \frac{NOAEL}{SED} x \frac{1}{2} x \frac{1}{3} = \frac{100\ x\ 10^{-3}}{0.0000016} x \frac{1}{2} x \frac{1}{3}\right)$
The Margin of Safety (MoS) when considering a 50% dermal absorption and utilizing the dose with no apparent toxic effect, extra default value (50%) due to no oral bioavailability data and default factor 3 (no 90-day study, but only 28-day) in the calculation is 128.
=> cosmetic ingredient is considered as safe, if MoS ≥ 100

LIST OF COMPATIBLE INGREDIENTS

INGREDIENT	CONCENTRATION
GLYCEROL	5% v/v
GLYCEROL + ETHANOL	5% v/v + 0.5 % v/v
EUSOLEX T-2000 + GLYCEROL + EUXYL PE9010	1.5% w/v + 3% v/v + 0.6% v/v
EUSOLEX 232 +GLYCEROL + EUXYL PE9010	1% w/v + 3% v/v + 0.6% v/v
EUSOLEX T-AVO + GLYCEROL + EUXYL PE9010	1.5% w/v + 3% v/v + 0.6% v/v
EUXYL	0,5% w/v
PROPLYLENGLYKOL	5% v/v
BUTYLENGLYKOL	5% v/v
ETHANOL	2% v/v
ETHANOL	10% v/v
ETHANOL	20% v/v
UREA	2% w/v
DISODIUM EDTA	0.2% w/v
BISABOLOL	1% w/v
PANTHENOL	1% w/v
VITAMIN C	1% w/v
PENTYLENGLYCOL	5% v/v
HYALURONIC ACID	0.1% w/v

LIST OF INCOMPATIBLE INGREDIENTS

INGREDIENT	CONCENTRATION
CHLOROFYLIN	0.1% w/v
ACETYLCYSTEIN	0.5% w/v

REFERENCES

1. ORNITZ, David M. a Nobuyuki ITOH. The Fibroblast Growth Factor signaling pathway. WIREs Developmental Biology. 2015, 4(3), 215-266. doi:10.1002/wdev.176

2. MATSUMOTO, Shigeru, Rica TANAKA, Kayoko OKADA, et al. The Effect of Control-released Basic Fibroblast Growth Factor in Wound Healing. Plastic and Reconstructive Surgery Global Open. 2013, 1(6) [cit. 2023-06-06]. doi:10.1097/GOX.0b013e3182a88787

3. AOKI, Shimpo, Mao FUJII, Toshinori FUJIE, et al. The efficacy of basic fibroblast growth factor-loaded poly(lactic- co -glycolic acid) nanosheet for mouse wound healing. Wound Repair and Regeneration. 2017, 25(6), 1008-1016 [cit. 2023-06-06]. doi:10.1111/wrr.12604

4. KANDA, Norikazu, Naoki MORIMOTO, Satoru TAKEMOTO, et al. Efficacy of Novel Collagen/Gelatin Scaffold With Sustained Release of Basic Fibroblast Growth Factor for Dermis-like Tissue Regeneration. Annals of Plastic Surgery. 2012, 69(5), 569-574 [cit. 2023-06-06]. ISSN 0148-7043. doi:10.1097/SAP.0b013e318222832f

5. YAO, Chengcan, Ping YAO, Hao WU a Zhengang ZHA. Acceleration of wound healing in traumatic ulcers by absorbable collagen sponge containing recombinant basic fibroblast growth factor. Biomedical Materials [online]. 2006, 1(1), 33-37 [cit. 2023-06-06]. ISSN 1748-6041. doi:10.1088/1748-6041/1/1/005

6. UCHI, Hiroshi, Atsuyuki IGARASHI, Kazunori URABE, et al. Clinical efficacy of basic fibroblast growth factor (bFGF) for diabetic ulcer. European Journal of Dermatology. 2009, 19(5), 461-468 [cit. 2023-06-06]. ISSN 1167-1122. doi:10.1684/ejd.2009.0750

7. OHURA, Takehiko, Toshio NAKAJO, Takahiko MORIGUCHI, et al. Clinical efficacy of basic fibroblast growth factor on pressure ulcers: Case-control pairing study using a new evaluation method. Wound Repair and Regeneration. 2011, 19(5), 542-551 [cit. 2023-06-06]. ISSN 10671927. doi:10.1111/j.1524-475X.2011.00726.

8. LIN, Wei-hong, Li-Jun XIANG, Hong-Xue SHI, et al. Fibroblast Growth Factors Stimulate Hair Growth through β -Catenin and Shh Expression in C57BL/6 Mice. BioMed Research International. 2015, 2015, 1-9 [cit. 2023-06-06]. ISSN 2314-6133. doi:10.1155/2015/730139

9. NASTO, Barbara. Biotech at the beauty counter. Nature Biotechnology. 2007, 25(6), 617-619. ISSN 1087-0156. doi:10.1038/nbt0607-617

10. ONO, Ichiro. A study on the alterations in skin viscoelasticity before and after an intradermal administration of growth factor. Journal of Cutaneous and Aesthetic Surgery. 2011, 4(2) [cit. 2023-06-06]. ISSN 0974-2077. doi:10.4103/0974-2077.85022

11. SARABIPOUR, Sarvenaz a Kalina HRISTOVA. Mechanism of FGF receptor dimerization and activation. Nature Communications. 2016, 7(1) [cit. 2023-06-06]. ISSN 2041-1723. doi:10.1038/ncomms10262

12. VIAÑA-MENDIETA, Pamela, Mirna Lorena SÁNCHEZ a Jorge BENAVIDES. Rational selection of bioactive principles for wound healing applications: Growth factors and antioxidants. International Wound Journal. 2022, 19(1), 100-113 [cit. 2023-06-06]. ISSN 1742-4801. doi:10.1111/iwj.13602

13. RAHROVAN, S., F. FANIAN, P. MEHRYAN, P., et al. Male versus female skin: What dermatologists and cosmeticians should know. International Journal of Women's Dermatology. 2018, 4(3), 122-130 [cit. 2023-06-06]. ISSN 23526475. doi:10.1016/j.ijwd.2018.03.002

14. patent: DVORAK, Petr, Pavel KREJCI, Lukas BALEK, et al. Thermostable fgf2 polypeptide, use thereof. EP, AU, SG, JP, KR, US, CA, BR, CN. WO 2017/089016 A1. 3.10.2016

15. DVORAK, Pavel, David BEDNAR, Pavel VANACEK, et al. Computer-assisted engineering of hyperstable fibroblast growth factor 2. Biotechnology and Bioengineering. 2018, 115(4), 850-862 [cit. 2023-06-06]. ISSN 0006-3592. doi:10.1002/bit.26531

16. UNGER, Ellis F., Shmuel BANAI, Matie SHOU, et al. Basic fibroblast growth factor enhances myocardial collateral flow in a canine model. Online. American Journal of Physiology-Heart and Circulatory Physiology. 1994, roč. 266, č. 4, s. H1588-H1595 [cit. 2023-11-10]. ISSN 0363-6135. doi:10.1152/ajpheart.1994.266.4.H1588

17. SCCS/1647/22. THE SCCS NOTES OF GUIDANCE FOR THE TESTING OF COSMETIC INGREDIENTS AND THEIR SAFETY EVALUATION. 12. Scientific Committee on Consumer Safety, 2023.

Enantis

Enantis is an innovative biotechnology company focused primarily on growth factors, which are among the most important biomolecules in the human body. Our goal is to enhance their low stability, making them more applicable in industries such as cosmetics and medicine.

The core values and uniqueness of Enantis lie in the full integration of the development process, from designing novel molecules to their optimization, characterization, and production. Our mission is to contribute to a healthier and more sustainable future through the development of innovative solutions.

Enantis s.r.o.
Kamenice 34, 625 00 Brno, Czech Republic
+420 511 205 286
enantis@enantis.com

The FGF2-STAB project for cosmetics is co-financed through the OPPIK-Aplikace 2020 program of the European Commission under the grant agreement number CZ.01.1.02/0.0/0.0/20_321/0023865.