# Clinical Evidence



PRODUCT, DESCRIPTION AND EVIDENCE REFERENCE: FS4-86 PUBLISH DATE: 12/04/2023

## RF

### **EYE LIFT GEL**

This potent fragrance-free lightweight eye treatment is formulated with peptides, stem cells, and natural antioxidant extracts like green tea, pomegranate, and red algae. It helps promote the creation of healthy, youthful-looking skin while maintaining its integrity, resulting in a firmer, more compact skin feel. With caffeine and licorice root, this rich lightweight gel cream also aids in brightening the under-eye complexion and reducing the appearance of dark circles. The appearance of eye bags and crow's feet will be reduced, and the entire eye area will be brighter, more illuminated, and have a more youthful, refreshed, and less tired look.

#### **KEY BENEFITS**

- Skin looks lifted with a reduced appearance of wrinkles.
- · Lessens the appearance of crow's feet.
- Improves skin luminosity by 150%.
- · Lessens swelling and puffiness in the eye area.
- Reduces the appearance of blemishes.
- Stimulates the production of new collagen.
- Calms and soothes irritated skin.
- Skin appears tighter, firmer, and more elastic.
- Skin looks more youthful, with a uniform and brighter complexion.
- Reduces the appearance of under-eye dark circles.
- · Diminishes the look of under-eye bags.
- Infused with powerful antioxidants that help reduce the signs of ageing.
- Enhances the quality and consistency of the skin's surface.
- Boosts moisture content in the skin.

#### **DIRECTIONS FOR USE**

Apply a small amount of product to the eye area. Massage gently. Avoid contact directly with the eye.

#### WARNINGS

For external use only. Avoid contact with eyes. If this occurs wash affected area thoroughly with water. If irritation occurs, discontinue use. Store this product below 40°C.

#### **INGREDIENTS**

Aqua, Glycerin, C15-19 Alkane, Propanediol, Sodium Acrylates Copolymer, Phenoxyethanol, Coco-Caprylate/ Caprate, Butylene Glycol, Lecithin, Camellia Sinensis Leaf Extract, Lactobacillus Ferment Lysate, Punica Granatum Extract, Glycyrrhiza Glabra Root Extract, Hydroxypropyl Methylcellulose, Tocopherol, Silica, Sodium Gluconate, Pullulan, Malus Domestica Fruit Cell Culture Extract, Helianthus Annuus Seed Oil, Ethylhexylglycerin, Lactobacillus Ferment, Yeast Extract, Leuconostoc/Radish Root Ferment Filtrate, Malachite Extract, Persea Gratissima Fruit Extract, Caffeine, Carbomer, Sodium Lactate, Xanthan Gum, Polysorbate 20, Porphyridium Cruentum Extract, Sodium Hyaluronate, Palmitoyl Tripeptide-1, Palmitoyl Tetrapeptide-7, CI 77891 (Titanium Dioxide), CI 77491 (Iron Oxide).

#### **ACTIVE INGREDIENTS**

Palmitoyl Tetrapeptide-7  $1.5_{mg}^{*}$ 

Palmitoyl Tripeptide-1 3<sub>mg</sub>\*

Malus Domestica Fruit Cell Culture Extract (Apple Stem Cell Extract) 1800, \*\*

Persea Gratissima Fruit Extract (Avocado Fruit Extract) 525<sub>ma</sub>\*

Camellia Sinensis Leaf Extract (Green Tea Extract) 0.5%

Glycyrrhiza Glabra Root Extract (Licorice Root Extract) 4000<sub>mg</sub> \*

Punica Granatum Extract (Pomegranate Extract) 0.5%

Caffeine 500<sub>mg</sub>\*
Sodium Hyaluronate 150<sub>mg</sub>\*

Malachite Extract 600<sub>mg</sub>\*

Yeast Extract (Yeast Protein) 900<sub>mg</sub>\*

Leuconostoc Radish Root Ferment Filtrate (Fermented Radish Root Extract) 800<sub>mg</sub>\*

Lactobacillus Ferment Lysate 0.5%

Porphyridium Cruentum Extract (Red Algae Extract) 150<sub>ma</sub>\*

Pullulan (Pullulan Polysaccharide) 1875<sub>ma</sub>\*

#### PALMITOYL TETRAPEPTIDE-1 & PALMITOYL TETRAPEPTIDE-7

#### Ingredient Claims:

Decreased wrinkle depth by up to 19.9%	Upregulates collagen synthesis for firmer, more elastic looking skin
Decreased wrinkle density by up to 32.9%	16% improvement in skin complexion
Skin appears up to 16% smoother	15.5% improvement in skin tone

#### Repair of the papillary dermis

28 female volunteers aged from 51 to 72 years, mean age 59. Twice daily application of cream containing 3% of Palmitoyl Tripeptides for 2 months to one half of the face and the forearm (inner and UV-exposed outer forearm) against placebo.

after 2 months	Inner Forearm	Outer Forearm
	-9.8%/TO up to -23%, p<0.01	-9.8%/TO up to -33%, p<0.01
THICKNESS	93% volunteers	86% volunteers
	-11%/placebo, p<0.01	-14.4%/placebo, p<0.01
	<b>+11.4%/TO</b> up to <b>+44%</b> , p<0.01	<b>+11.5%/TO</b> up to <b>+45%</b> , p<0.01
DENSITY	68% volunteers	82% volunteers
	+15.2%/placebo, p<0.01	<b>+15.1%/placebo</b> , p<0.01
AGE GAIN	-3.8 YEARS	-5.5 YEARS

#### Anti-wrinkle efficacy, skin tone and elasticity

23 female volunteers aged from 42 to 67 years / Twice daily application on one half of a cream containing 3% of Palmitoyl Tripeptides against placebo, for 2 months. Assessment of the anti-wrinkle efficacy by profilometry, cutometry and photography compared to TO

Compared to TO (%)	Palmitoyl Tripeptides	Placebo
Surface occupied by deep wrinkles	-39.4**	4.3 <sup>n.s.</sup>
Main wrinkle density	-32.9**	-9.9n.s.
Main wrinkle average depth	-19.9**	-3.2 <sup>n.s.</sup>
Main wrinkle average volume	-23.3**	-8.7*
Roughness	-16.0**	-1.4 <sup>n.s.</sup>
Complexity (Lifting effect)	-16.2**	4.2 <sup>n.s.</sup>
Elasticity	+5.5*	<b>4.1</b> n.s.
Skin tone	+15.5**	6.5 <sup>n.s.</sup>





n.s. : non-significant \*: significant/TO (p<0.05) \*\*: significant/TO (p<0.01)

## Variation in DEJ macromolecules/papillary dermis with age; effect of **Palmitoyl Tripeptides** on these components 5 days after topical application

	Collagen I	Collagen IV	Collagen VII	Collagen XVII	Nidogen-1
Variation with age (in %)	( <b>↓</b> )-8%; p<0.2	( <b>↓</b> )-11%; p<0.05	( <b>↓</b> )-17%; p<0.01	( <b>1</b> )-31%; p<0.01	( <b>↓</b> )-15%; p<0.01
Placebo (AFU)	20.80 + 4.02	10.51 + 2.95	12.56 + 2.01	4.64 + 1.05	5.09 + 2.55
Palmitoyl Tripeptides 3% (AFU)	23.79 + 2.96	11.18 + 2.28	14.99 + 3.75	5.37 + 2.29	5.83 + 4.04
Variation (%) vs. placebo	(†)+14.40%; p<0.01	(†) +6.4%; p<0.05	(†)+20.30%; p<0.01	(†) +15.84%; p<0.01	(†) +14.49%; p<0.01

AFU: Arbitrary Fluorescence Unît; (1) = increase ( $\downarrow$ ) = decrease

Link: Data on file

After 2 months of daily application of Palmitoyl Tripeptides, the following points were observed:

- reduction in the mean depth of the main wrinkle (-19.9%) and in its volume (-23.3%).
- reduction in roughness (-16%) and complexity (-16.2%), a surface "lifting" parameter.
- decrease in the area occupied by deep wrinkles (>200  $\mu$ m) (-44%), giving rise to a decrease in density (-32.9%).
- increase in skin tone (+15.5%).

A blind, randomised clinical study with 28 volunteers twice daily applying cream including the active compound to half their face and one of their forearms and a placebo cream to the other half of the face and other forearm confirmed anti-wrinkle efficacy, reduction of wrinkle depth, volume and density, skin roughness and complexity, as well as a

decrease of the area occupied by deep wrinkles, and an increase in skin tone.

#### Sources

https://www.mdpi.com/2079-9284/4/2/16#B16-cosmetics-04-00016

#### PALMITOYL TRIPEPTIDE-1

The various forms of peptides act upon collagen found in the body and particularly the skin. The most abundant form of collagen in the body is type collagen I, which is the collagen primarily responsible for repairing the skin. Collagen type III is found alongside collagen type I and works much in the same way, though it is not as tough as collagen I. Palmitovl

Tripeptide–1 mimics the relationship between the growth factors involved in the skin's healing process and the production of collagen. Essentially, Palmitoyl Tripeptide-1 tricks the skin into producing more collagen to repair the skin, improve elasticity and

minimise the appearance of fine lines and wrinkles. Palmitoyl Tripeptide—1 is a powerful skincare ingredient to combat aging, but like most skincare ingredients it works more effectively when used in combination with other anti-ageing peptide ingredients. When used as part of a good skin-care routine, Palmitoyl Tripeptide—1 can help skin repair damage by stimulating collagen production. The result is younger, smoother and stronger skin.

In a study with 15 women, a cream containing palmitoyl tripeptide-1 was applied twice daily for four weeks, leading to statistically significant reductions in wrinkle length, depth and skin roughness. Another study applied both vehicle and palmitoyl tripeptide-1 to the skin of 23 healthy female volunteers for four weeks.

#### Sources

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#### PALMITOYL TETRAPEPTIDE-7

Palmitoyl Tetrapeptide-7 (It was also formerly known and marketed as Palmitoyl Tetrapeptide-3. Palmitoyl Tetrapeptide-7 consists of a short chain of four amino acids (a.k.a. GQPR peptide or glycineglutamineproline-arginine) connected to palmitic acid.

Palmitic Acid is a fatty acid added to improve the peptide's oil solubility and thus skin penetration. Palmitoyl Tetrapeptide-7 serves as an anti-inflammatory after exposure to UVB-irradiation. In vivo reflectance confocal microscopy studies indicated that a blend of Palmitoyl Oligopeptide and Palmitoyl Tetrapeptide-7 enhanced the extracellular matrix structure compared to placebo. Sixty healthy photoaged volunteers were tested over 12 months with a formulation containing Palmitoyl Tetrapeptide-7. A reduction of facial wrinkles was documented by this long-term use.

Palmitoyl Tetrapeptide-7 used in conjunction with Palmitoyl-Oligopeptide. They can boost the growth of the connective tissues and naturally increasing the production of collagen in the skin; when the production of collagen is increased, the skin can heal and rejuvenate itself.

It serves as an anti-inflammatory after exposure to UVB-irradiation. In vivo reflectance confocal microscopy studies indicated that a blend of palmitoyl oligopeptide and palmitoyl tetrapeptide-7 enhanced the extracellular matrix structure compared to placebo.

A reduction of facial wrinkles was documented by this long-term use. Better skin appearance was related to the deposition of fibrillin-rich microfibrils in the papillary dermis of treated skin.

#### Sources

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#### MALUS DOMESTICA FRUIT CELL CULTURE EXTRACT

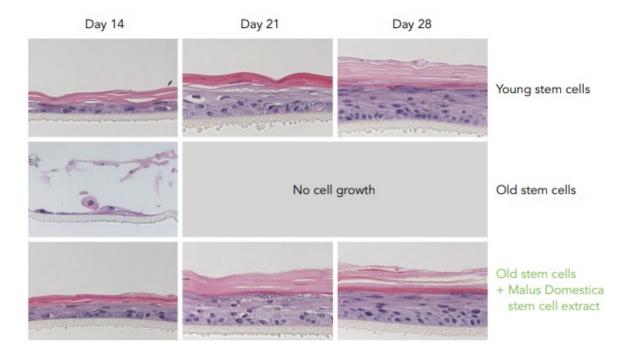
Ingredient Claims:

Skin feels up to 27% thicker	11.1% reduction in the appearance of crow's feet
Skin feels 6.9% smoother	

A revolutionary technology to protect skin stem cells - Malus Domestica (Apple Stem Cell Extract) is a liposomal preparation based on the stem cells of a rare Swiss apple. Uttwiler spätlauber is an endangered apple variety that was well-known for its excellent storability and thus its longevity potential. The protection of human stem cells by Malus Domestica has been shown by various experiments. Other studies demonstrated its age delaying and anti-wrinkle effects. It rejuvenates ageing skin by stimulating ageing skin stem cells. The plant extract has been shown to lessen the appearance of unsightly wrinkles. Clinical trials show that this unique formulation increases the longevity of skin cells, resulting in skin that has a more youthful and radiant appearance. Plant regeneration at the cellular and tissue level is a unique process. Similar to animals, the stem cells in plants have properties that help stimulate and regenerate plants after injury. The unique properties of plant stem cells have been a recent area of interest and focus both in developing new cosmetics and studying how these extracts/phytohormones will influence animal skin. Studies show that apple stem cells boost production of human stem cells, protect the cell from stress and decreases wrinkles. The internal fluid of these plant cells contains components that help to protect and maintain human stem cells. Apple stem cells contain metabolites to ensure longevity as the tree is known for the fact that its fruit keep well over long periods of time.

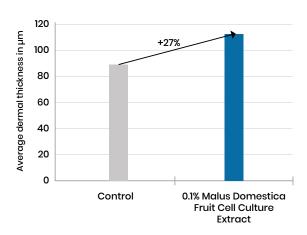
In the presence of the 0.1% Malus Domestica Fruit Cell Culture Extract, the study shows skin stem cells keep their ability to proliferate and undergo the complex process of stratification and differentiation for a longer period of time. Therefore, the Malus Domestica Fruit Cell Culture Extract helps the epidermal stem cells to retain their capacity to build new tissues.

Maintenance of the capacity to form a 3D epidermis



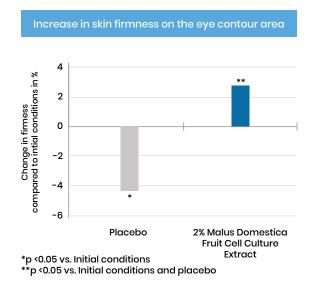
0.1% Malus Domestica Fruit Cell Culture Extract increased dermal thickness by 27% compared to the control. It also improved the structure and the regularity of the basal keratinocyte layer in direct contact with the basement membrane.

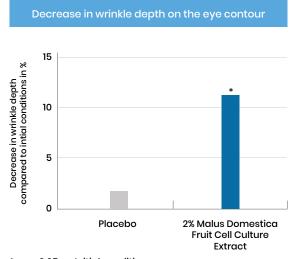
#### Increased thickness of the Dermis



Clinical study involving twenty-one women aged from 35 to 56 years. Volunteers either applied a cream containing 2% Malus Domestica Fruit Cell Culture Extract or a placebo cream twice daily for 28 days to the 'crow's feet' area on one-half of their face each.

Results showed that the treatment with 2% Malus Domestica Fruit Cell Culture significantly increased skin firmness. Meanwhile, compared to the placebo treatment, skin firmness was increased by 6.9% after 28 days of treatment.





\* p <0.05 vs. Initial conditions

Study using 2% Malus Domestica Fruit Cell Culture was reduced the wrinkle depth of 'crow's feet' by 11.1% compared to initial conditions.

#### Sources:

Data on file

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5674215

#### PERSEA GRATISSIMA FRUIT EXTRACT (AVOCADO FRUIT EXTRACT)

Ingredient Claims:

Stimulates antioxidant activity and protect stems cells from stress	Improves skin luminosity by 150%
Reduces appearance of dark circles by 180%	Reduces puffiness by 12.5%
Skin appears brighter and firmer	

Native to Mexico: consumed 10,000 years ago by Aztecs & Mayas, imported to Europe in the 17th century.

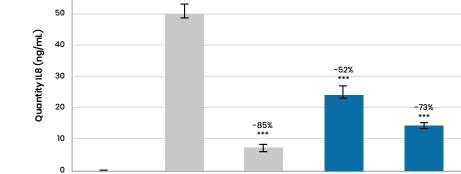
#### Key Benefits:

- Lightens complexion, reduces dark circles, reduces eye bags.
- Acts on: Inflammation, Pigmentation irregularity, Vascular and lymphatic permability, Blood circulation and Fatty deposits.
- It inhibits tyrosinase activity and reduces adipocytes size.
- Reduces appearance of eye bags and dark circles
- Antioxidant
- Reduce appearance of wrinkles
- · Improved skin elasticity

Reduced Interleukin 8 (IL8) activity, reduced synthesis of Prostaglandin E2 (PGE2) (induces skin ageing).

Control

60



\$\$\$

PMA 0.1ug/mL

IL8 dosage

Dexamethasone

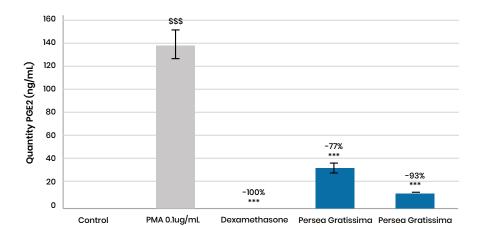
PGE2 dosage

Persea Gratissima Persea Gratissima

Keratinocytes incubated for 24hr with Persea Gratissima Oil vs Dexaméthasone

Stimulation with PMA (Phorbol 12-Myristate 13-Acetate) for 24hr

\$\$\$ p<0.001 vs temoin no stimulated \*\*\* p<0.001 vs PMA



10-7M

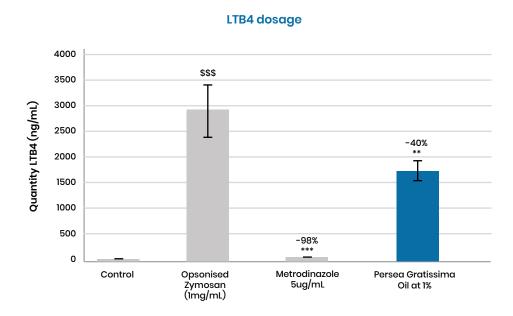
Oil at 0.5%

Oil at 1%

Reduced Oedema formation-reduces inflammation.

LTB4: chemotactic factor

Chemotactic factor activated in response to inflammation, increases vasular permeability.

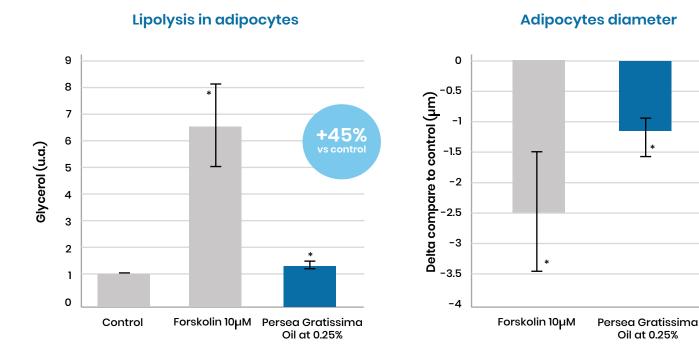


Human neutrophils incubated with Persea Gratissima Oil or Métronidazole at 5µg/mL, for 15 minutes

Stimulation by opsonised zymosan (1mg/ml) for 10 minutes

\$\$\$ p<0,001 vs control \* p<0.05 \*\* p<0.01 vs zymosan

Stimulates lipolysis to reduce puffiness



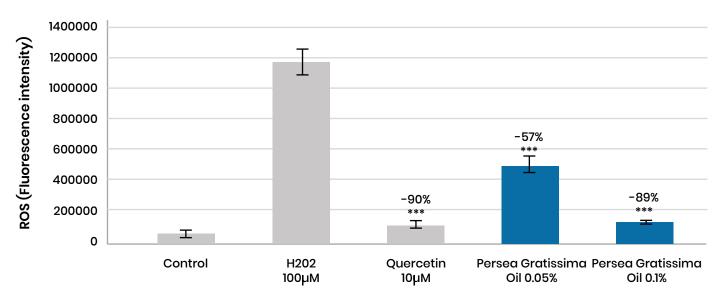
Mature adipocytes treated for 4hr with Persea Gratissima Oil or Forskolin, Glycerol released measurement

Measure of adipocyte diametre using a cell-size counter

<sup>\*</sup> p<0.05

Stimulates antioxidant activity and protects stem cells from oxidative stress.

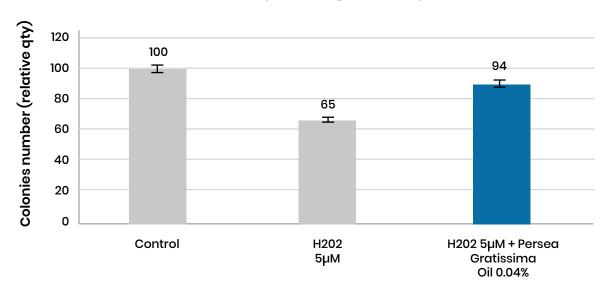
### **ROS Dosage in keratinocytes**



Keratinocytes pre-treated for 24hr then treated for 20mins by H202.

\*\*\* p<0.001

#### **Colony Forming Efficiency**



Epidermal progenitor cells exposed to H202; 5µM for 15mins. Assessment of colony-forming capacity.

#### Conclusion:

- Increase in Microcirculation
- Decrease in inflammation
- Decrease vascular & lymphatic permeability
- Decongestion
- Oedema reduction



#### Lightening Effect

- Decrease Melanogenesis
- Decrease Tyrosinase



Decrease fatty deposits

- Increase Lipolysis
- Adipocytes diametre

#### Clinical Case Study 1

#### Population

- 20 healthy female volunteers
- 22 to 66 years old (average age 40 years old)

#### Inclusion Criteria

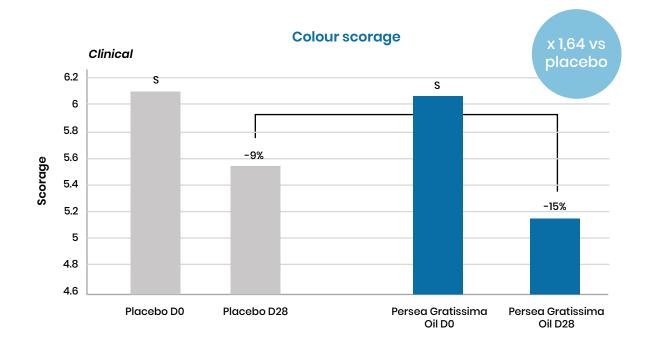
- Randomised double blind study vs placebo
- Dark circle on the face

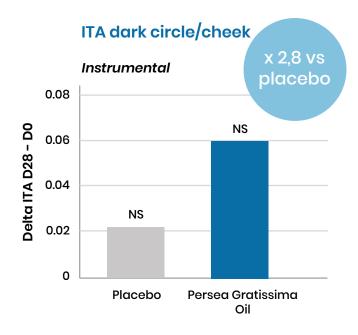
#### Protocol

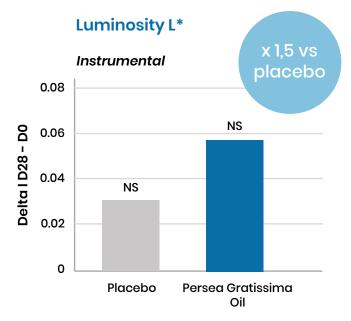
- Use of a cream containing 3% of Persea Gratissmia Oil or a placebo
- Hemi face
- Twice a day
- During 28 days

#### Colour Results

Persea Gratissmia Oil decreases the intensity of dark circles.

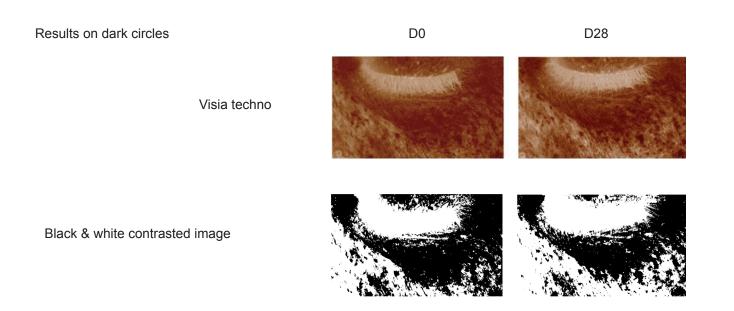






Colour of dark circles (skin colour infraorbital)

- Score 0: skin colour similar to other skin areas
  - Score 9 : dark circle very intense and visible



#### Clinical Case Study 2

#### Population

- 23 healthy female volunteers
- 44 to 70 years old (average age 63 years old)

#### Inclusion Criteria

Eye bags on the face (Bazin scale superior to grade 2)

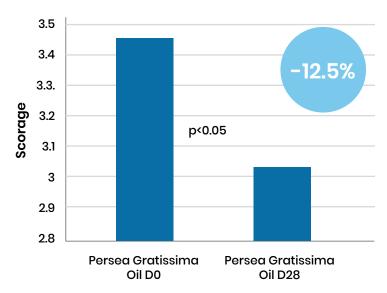
#### Protocol

- Use of a cream containing 3% of Persea Gratissmia Oil
- Face
- Twice a day
- During 28 days

#### **Puffiness Volume**

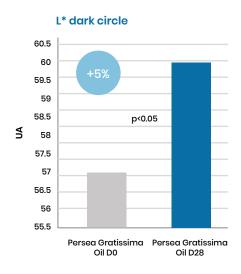
Results on puffiness

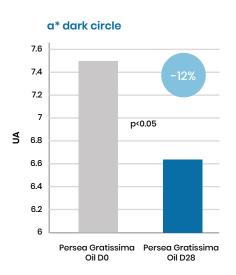
Persea Gratissmia Oil reduces the volume of puffiness

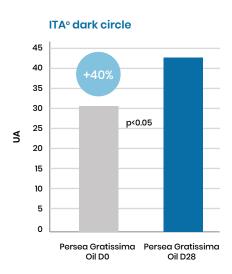


Results on dark circles

Persea Gratissmia Oil lightens the dark circles







Link: Data of file

Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6887779/

Avocado Oil is rich in Vitamins A, D and E and can penetrate quickly into the lower skin layers to promote healing, skin regeneration and protection from the ageing effects of UV light and pollution. Used topically, vitamin-rich Avocado Oil smooths wrinkles, helps to tighten the skin and diminish blemishes. It is also gentle enough to be used on dry, ageing, rough or sensitive skin.

The main chemical constituents of Avocado Oil are: Palmitic Acid, Palmitoleic Acid, Stearic Acid, Oleic Acid, Linoleic Acid, Alpha Linoleic Acid. These chemical constituents all carry their own set of beneficial skin properties: Palmitic Acid has emollient properties; Palmitoleic Acid helps delay the appearance of premature ageing, moisturises and tightens skin, enhances skin complexion and skin elasticity; Stearic Acid has cleansing properties and can balance out excess sebum and soften skin; Oleic Acid helps skin suppleness and helps reduce the signs of ageing Linoleic Acid has anti-inflammatory properties and promotes moisture retention in skin.

#### Sources

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6887779/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3249906/https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6600360

#### CAMELLIA SINENSIS LEAF EXTRACT - GREEN TEA EXTRACT

Ingredient Claims:

Reduces oxidative stress in the skin to minimise the signs of ageing	Protects the skin against damaging pollutants
Improves the appearance of sundamaged skin	Skin feels smoother and more even
Inhibits the activity of collagen and elastin degrading enzymes	Improves skin microcirculation for healthier-looking skin
Soothes irritated skin	

Camellia Sinensis Leaf Extract - Green Tea Extract

#### Ingredient Claims:

Research has established that topical application of green tea leaves or extracts have many benefits for skin, including anti-ageing properties. The polyphenols in green tea possess potent antioxidant and skin-soothing properties, and show significant promise for improving the appearance of sun-damaged skin. Epigallocatechin gallate (EGCG) is one of the active constituents of green tea believed to be responsible for its many health and appearance benefits, both orally and topically. The primary benefit of green tea is an antioxidant boosting skin against environmental pollutants. Research also shows that the catechins in Green Tea Extract act as a sunblock and as a way to reduce signs of ageing in sun-damaged skin.

Green tea is an anti-inflammatory agent, so it will soothe skin and help prevent redness.

#### Antioxidant:

 Tea Catechins, regarded as the most important antioxidant substance in the human diet, contribute a lot to the beneficial effects to the skin. Oxidative stress is the most important factor in the aging of the skin. Natural oxidants like this are helpful in the prevention of this process. Polyphenols in this extract can have moisturizing and protective effects. Skin roughness is significantly reduced with its use.

#### Photoprotective Activity:

• Ultraviolet radiations ranging from 280-400 nm are very detrimental to the skin. This extract can absorb ultraviolet radiation in harmful range and may also have scavenging properties for radicles produced by UV radiations.

#### Anti-ageing:

Multiple enzymes including collagenases, hyaluronidase, metalloproteinases, lipoxygenases can have a
destructive effect on skin cement lipid. So, Camellia Sinensis by inhibiting these enzymes delays the aging of the
skin by preserving hyaluronic acid, elastin, collagen important for the skin. Alkaloids, phenols, and catechins are
effective in preventing the formation of cellulite thus further aiding anti-ageing objective.

#### Anti-Inflammatory:

By inhibiting platelet aggregation, cyclooxygenase (COX-1), and thromboxane synthase (TXAS) production in
platelet, it produces anti-inflammatory effect even stronger than commonly used non-steroidal anti-inflammatory
drug aspirin. It improves skin microcirculation and protects intracellular cement lipids.

Sebum Production/Acne:

Oily skin, a result of excessive sebum production, accompanied by the problem of acne can be solved by the topical application of its extract. It helps reduce sebum production and have anti-greasy effect too.

#### Conclusion:

Camellia Sinensis and its extracts can improve skin regeneration by its anti-oxidant, anti-inflammatory, and toning properties. It is strongly soothing, protects against harmful environmental influencers, eliminates excess sebum, and improves skin hydration.

#### Sources:

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#### GLYCYRRHIZA GLABRA ROOT EXTRACT (LICORICE ROOT EXTRACT)

#### Ingredient Claims:

	Protects the skin from environmental stressors such as pollution and UV
Helps the skin retain moisture, skin appears fuller and more hydrated	Reduces the appearance of blemishes

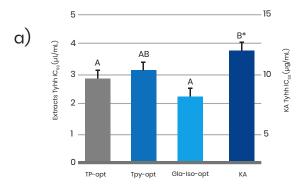
Glycyrrhiza Glabra Root Extract, also known as licorice root extract, is a natural plant-based ingredient that has been used for centuries in traditional medicine and skincare. Here are some of the skin benefits of Glycyrrhiza Glabra Root Extract:

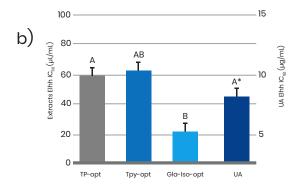
- Anti-inflammatory: Glycyrrhiza Glabra Root Extract has anti-inflammatory properties that can help to soothe and calm irritated skin. This makes it a popular ingredient in skincare products designed for sensitive skin.
- Brightening: Glycyrrhiza Glabra Root Extract can help to brighten the skin by inhibiting the production of melanin, the pigment that gives skin its colour. This makes it a popular ingredient in skincare products designed to address dark spots and uneven skin tone.
- Anti-aging: Glycyrrhiza Glabra Root Extract contains antioxidants that can help to protect the skin from
  environmental stressors, such as UV radiation and pollution. This can help to reduce the appearance of fine lines
  and wrinkles and prevent premature ageing.

- Moisturising: Glycyrrhiza Glabra Root Extract is a natural humectant, which means it can attract and retain moisture in the skin. This can help to improve the overall hydration and plumpness of the skin.
- Acne-fighting: Glycyrrhiza Glabra Root Extract has been shown to have antibacterial properties that can help to reduce the growth of acne-causing bacteria on the skin.

A green ultrasound-assisted extraction (UAE) method using glycerol/water mixtures for extraction of licorice (Glycyrrhiza Glabra) bioactive constituents was developed in this study. The response surface method, according to the Box-Behnken design, was employed to optimize the extraction parameters: glycerol concentration (X1), temperature (X2), and the amount of herbal drug used in the production (X3). The responses were content of total phenols (TP), TP extraction efficiency (TPy) and the content of licorice characteristic constituents, glabridin (Gla) and isoliquiritigenin (Iso). Response surface analysis predicted the optimal extraction conditions for maximized amounts of TP, Tpy, Gla, and Iso. The extracts were prepared using the calculated conditions. The analysis of the selected constituents confirmed the validity of the model. Furthermore, biological activity of the extracts was tested. The results demonstrate that UAE using glycerol is a fast and efficient method for preparation of extracts with excellent radical scavenging, Fe2+ chelating and antioxidant activity. Furthermore, the observed notable tyrosinase and elastase inhibitory activity of the extracts, as well as their anti-inflammatory activity, indicate the anti-aging properties of the investigated extracts. The fact that the extracts were prepared using the safe, cosmetically active solvent, glycerol, makes them suitable for direct use in specialised cosmeceutical formulations.

Produced from the roots and rhizomes of Glycyrrhiza glabra. It contains saponins, flavonoids, coumarins and triterpenoids. The polysaccharide fraction of licorice has shown remarkable immunomodulatory activity, especially by strengthening phagocytosis in the endothelial reticular system and stimulating interferon production. Glycyrrhizin has long demonstrated its strengthening action on hydrocortisone anti-inflammatory activity in rats. Other flavonoid components of licorice root, such as liquiritoside, have also shown in vitro anti-inflammatory activity.





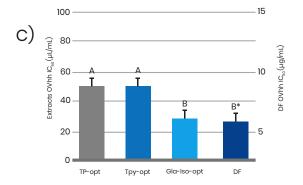


Figure 1. Tyrosinase (a) and elastase (b) inhibitory, and anti-inflammatory (c) activity of the extract and positive controls KA (Kojic Acid), UA (Ursolic Acid), and DF (Diclofenac). Different uppercase letters indicate statistical significance (p <0.05). Asterisk (\*) indicates that the  $IC_{50}$  unit is placed on the right y-axis.

Licorice root contains numerous bioactive natural products, many of which are potent cosmeceutical ingredients. In this work, the UAE method for preparation of licorice root bioactive extracts was optimized. The extraction was performed using mixtures of water with glycerol, a biodegradable, safe, cosmetically active solvent. The prepared extracts displayed excellent radical scavenging, Fe2+ chelating, and antioxidant activity. In addition, tyrosinase and elastase inhibitory activity of the extracts, as well as their anti-inflammatory activity, indicated excellent anti-aging properties. Such attractive array of skin-related biological activities makes glycerolic licorice extracts promising constituents of specialized cosmeceutical formulations.

Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6826613/

#### PUNICA GRANATUM EXTRACT (POMEGRANATE EXTRACT)

Ingredient Claims:

Skin lifting and tightening effect	Helps to prevent the formation of wrinkles
Protects the skin from oxidative damage	

Pomegranate is a juicy, bright red fruit that is considered a superfruit because of its unique antioxidant benefits as well as its high nutritional value. A distinct pomegranate extract which is extracted along with its high molecular weight carbohydrates. When applied on the skin, this ingredient provides immediate tightening and lifting benefits that help reduce the appearance of sagging and wrinkles.

#### Sources

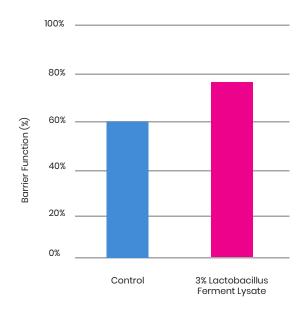
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#### LACTOBACILLUS FERMENT LYSATE

Ingredient Claims:

Supports the skin's microbiome	17% improvement in skin barrier function
Calms and soothes irritated skin	Improves skin radiancy
Improves skin texture	Reduces appearance of fine lines and wrinkles
Supports renewal of the epidermis	

Lactobacillus ferment lysate keeps the microbiome in balance while increasing skin tone and elasticity, minimising wrinkles, providing deep hydration and increasing cell turnover. It also helps to reduces redness and irritation.



Treatment with Lactobacillus Ferment Lysate clearly leads to a better barrier function.

Lactococcus Ferment Lysate, based on a lysate of Lactococcus lactis, to stimulate the skin's self-renewal effectively. This probiotic lactic acid–producing bacterium is grown under specific conditions, after which the obtained cells are lyzed, a process involving the killing and destruction of the bacterial cells.

Probiotic bacteria are well-established in the food industry, and their benefits for the human body are described in many scientific, peer-reviewed papers. In the gut they beneficially influence the composition and metabolic activity of the endogenous

bacteria, and some probiotic strains are even able to inhibit the growth of pathogenic bacteria. Probiotic bacteria are also reported to be able to modulate the immune

system, essentially improving immunocompetence and, therefore, our body's ability to

adapt to negative influences. Interestingly, it is not the whole living probiotic bacterial cell which is needed for the latter activity, it is the constituents and metabolites of these bacteria which are essential. A product obtained from a lysate of Lactococcus lactis, as Lactococcus Ferment Lysate, which essentially contains the cell debris of this bacterium – such as cell fragments, like DNA, metabolites, cytoplasmic compounds, and cell wall materials – should show and, in the studies performed, has shown that it is able to improve both the skin renewal processes and the processes involved in the skin's adaptation to negative influences.

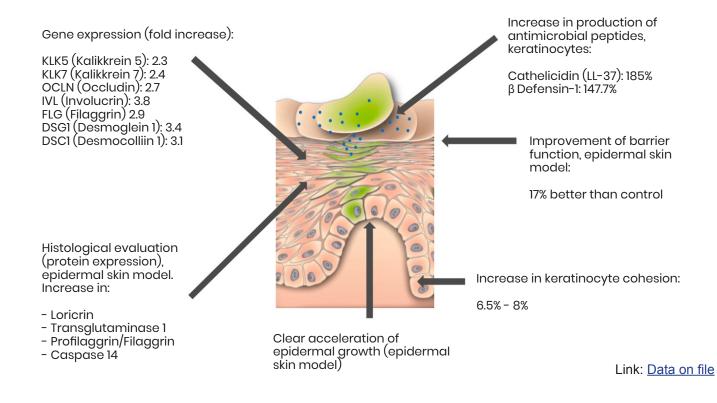
Lactobacillus Ferment Lysate helps to support the skin's microbiome, which is the collection of microorganisms that live on the surface of the skin. A healthy microbiome can help to protect the skin from harmful bacteria and maintain a healthy skin barrier.

Lactobacillus Ferment Lysate has anti-inflammatory properties that can help to calm and soothe the skin. This makes it useful for people with sensitive or reactive skin.

Lactobacillus Ferment Lysate can help to improve the skin's barrier function, which is important for maintaining healthy and hydrated skin. It helps to strengthen the skin's natural defence system, reducing moisture loss and keeping the skin hydrated and supple.

In addition, Lactobacillus Ferment Lysate has been shown to help improve skin radiance and overall skin health. It helps to improve skin texture, reduce the appearance of fine lines and wrinkles, and improve the overall brightness and clarity of the skin.

Lactococcus Ferment Lysate was shown to be able to accelerate the growth of the epidermal skin models, indicating that it is able to support the renewal processes in the epidermis. Additionally, it was shown that, by elevating the production of transglutaminase 1, (pro)filaggrin, and caspase-14, Lactococcus Ferment Lysate has a significant influence on the quality of the skin renewal process, as these molecules are essential for the quality of the skin. This observation was further supported by the assessment of the quality of the barrier function by topically applying SDS on the epidermal skin models, where the models which were treated with Lactococcus Ferment Lysate clearly showed a better barrier function.



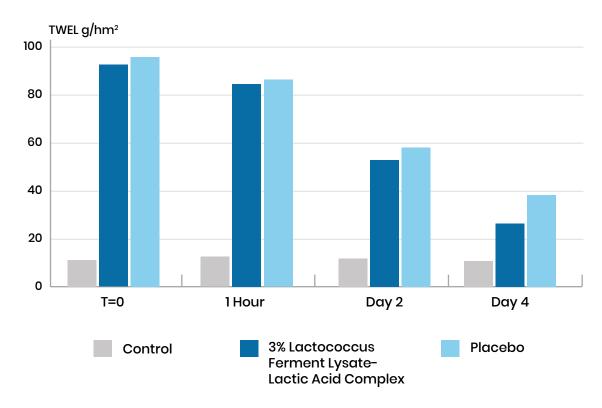


Fig. 15: Simulation of barrier recovery

Sources

Link: Data on file

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#### **CAFFEINE**

Ingredient Claims:

Reduces appearance of dark circles	Reduces appearance of bags under the eyes
Reduces puffiness around the eyes	Diminished appearance of expression lines around the eyes

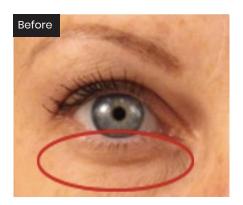
Collagen degradation occurs earliest around the eyes where skin is thinnest, making it imperative for products to treat the damage that causes bags under the eyes. By including caffeine, the product has the ability to reduce puffiness and diminish the appearance of the bags that emerge under the eyes. Caffeine's vasoconstrictive properties help reduce puffiness due to the ability to make blood vessels smaller. Additionally, its diuretic properties help deflate puffiness, increase circulation and minimize dark circles that form under the eyes. Furthermore, caffeine also provides antioxidant benefits that aid in the reduction of photo-agieng.

Now there's a non-surgical solution for treating the delicate eye area: An invigorating cream complex that can erase the signs of ageing.

To test the efficacy a three week in-vivo study was conducted. Ten subjects (Male & Female) between the ages of 24 and 45 were asked to apply the product on the right periorbital area of their faces twice a day for 3 weeks.

Pictures were taken at the start of the study and after the third week. As shown in figures 1 and 2, this product is capable of significantly reducing the appearance of bags under the eyes as well as dark circles after a 3-week period. As indicated with red ovals on both figures, wrinkles as well as expression lines were also significantly diminished by continued use of the product.

Figure 1:



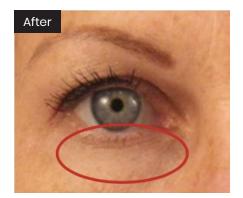


Figure 2:





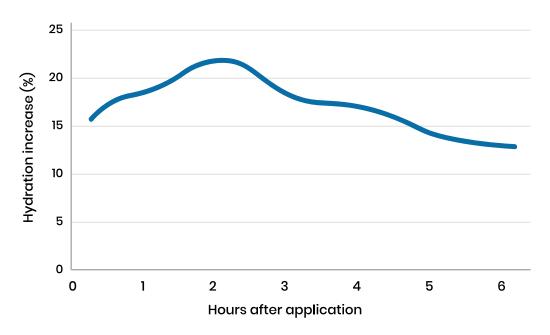
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#### **SODIUM HYALURONATE**

Ingredient Claims:

Boosts skin hydration	Supports the skin barrier
Promotes wound healing	Protects the skin from environmental damage
Skin feels smoother and tighter	Supports collagen and elastin formation

## Results: Up to 25% increase of skin hydration 2 hours after application



#### In vitro

High-molecular-weight (up to 2000 kDa) Sodium Hyaluronate improves skin hydration and elasicity when compared to placebo.\*

#### Study

0.025% Sodium Hyaluronate (1.4 MDa) in an emulsion vs placebo 8 Volunteers

Parameter: skin hydration (Corneometer CM 820 PC)

Link: Data on file

Sodium Hyaluronate is the salt form of Hyaluronic Acid, a water-binding ingredient that has the ability to fill the spaces between the connective fibres known as collagen and elastin. Hyaluronic Acid hydrates and separates the skin, allowing it to retain water and create a plumping effect. Sodium Hyaluronate has been used for moisturisation and wound healing since its discovery in the 1930s. It is comprised of small molecules that penetrate the skin easily and can hold up to 1000 their own weight in water. Because the skin naturally loses its water composition as it ages (going from 10% - 20% water to less than 10%).

Link: Data on file

Hyaluronic Acid and Sodium Hyaluronate can replace some of the water lost in the dermis, and potentially fight wrinkles and other signs of ageing. Because of its relatively high molecular weight it is not absorbed following application to the skin. Instead, it forms a thin, light, permeable, invisible, viscoelastic surface film. This fixes the moisture on the surface of the skin. The Hyaluronic Acid (HA) film supports the skin's natural protective mechanism. Since it is an excellent water reservoir leading to a perceptible and visible improvement in skin condition.

#### Sources

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3583886

#### MALACHITE EXTRACT

Ingredient Claims:

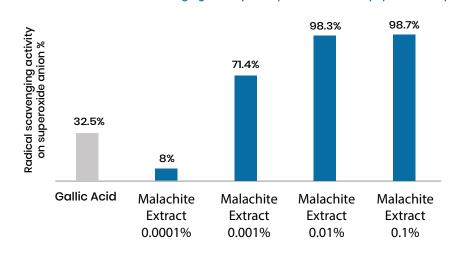
Protects skin cells from environmental damage to reduce the signs of ageing	Neutralises harmful pollutants to prevent skin damage
	Promotes collagen production to improve the skin's elasticity

Malachite is a copper-rich, semi-precious stone originating from Central Africa. Well known for its detoxifying properties, malachite is hydrated copper carbonate and possesses the following benefits for the skin:

- Antioxidant: Malachite extract is a potent antioxidant that can help to protect the skin from damage caused by free radicals. Free radicals are unstable molecules that can damage skin cells and contribute to the signs of ageing.
- Anti-inflammatory: Malachite extract has been shown to have anti-inflammatory properties, which can help to soothe and calm irritated skin. This can be particularly beneficial for people with sensitive or acne-prone skin.
- Detoxifying: Malachite extract can help to detoxify the skin by neutralizing harmful pollutants and toxins that can accumulate on the skin and contribute to skin damage and ageing.
- Moisturising: Malachite extract can help to improve skin hydration by retaining moisture and preventing moisture loss. This can help to improve the overall texture and appearance of the skin.
- Regenerating: Malachite extract has been shown to stimulate cell regeneration and promote collagen production, which can help to improve skin elasticity and reduce the appearance of fine lines and wrinkles.

### CELLULAR PROTECTION Measure of the quenching activity on free radicals

### PROTOCOL: Measure of the radical scavenging activity on superoxide anion, by spectrometry



Malachite Extract protects cells against free radicals damage with a dose-dependent effect

Link: Data on file

#### YEAST EXTRACT

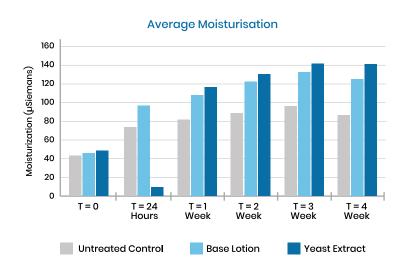
Ingredient Claims:

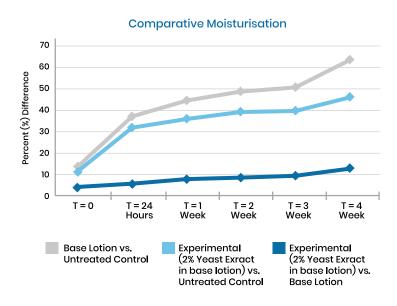
Protects the skin from damaging pollutants	Improves skin complexion
Reduces appearance of dark spots	Improves skin texture

By helping to reduce the amount of oxidative stress that occurs on the skin, the benefits of yeast extract can induce a calming effect that can help soothe and alleviate problematic skin. The health benefits of yeast extract are directly related to its high nutrient content, including antioxidants which are capable of neutralising harmful free-radicals that are present in the environment. This protective mechanism makes it perfect for cosmetics as it not only helps to maintain the skin's quality and texture, but also allows skin to retain moisture. Yeast also contains a number of beneficial ingredients including proteins, minerals, antioxidants and a variety of vitamins.

Containing beta glucan, yeast extract is highly moisturising that is also a natural source of antioxidant compounds combined with the ability to soothe skin and enhance skin barrier function.

Figure 1: Improved moisturisation compared to base lotion and control.





Sources

Link: Data on file

https://pubmed.ncbi.nlm.nih.gov/10188114/

https://bit.ly/2Ph7f7

#### LEUCONOSTOC RADISH ROOT FERMENT FILTRATE (FERMENTED RADISH ROOT EXTRACT)

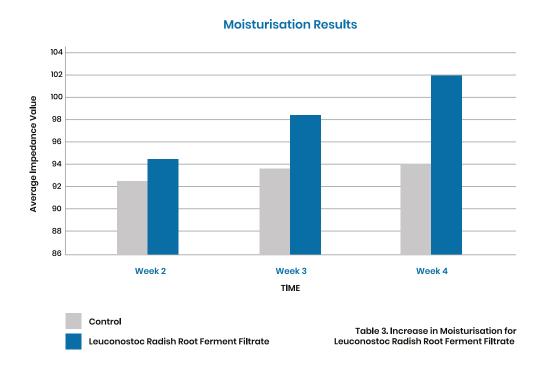
Ingredient Claims:

	Helps to prevent the growth of harmful bacteria which cause blemishes
Soothes irritated skin	Gently exfoliates the skin for a more radiant complexion

Leuconostoc radish root ferment filtrate is a natural antimicrobial ingredient that is derived from fermented radish roots. It has become a popular ingredient in skincare products due to its ability to act as a preservative and provide several benefits for the skin. Here are some of the skin benefits of Leuconostoc radish root ferment filtrate:

- Natural preservative: Leuconostoc radish root ferment filtrate has antimicrobial properties that make it an effective natural preservative in skincare products. This can help to extend the shelf life of the product without the use of harsh synthetic preservatives.
- Moisturising: Leuconostoc radish root ferment filtrate is a humectant, which means it has the ability to attract and
  retain moisture in the skin. This can help to improve the overall hydration and plumpness of the skin.
- Gentle exfoliation: Leuconostoc radish root ferment filtrate contains natural enzymes that can help to gently
  exfoliate the skin, removing dead skin cells and promoting a smoother, more radiant complexion.
- Antimicrobial: Leuconostoc radish root ferment filtrate has antimicrobial properties that can help to prevent the growth of harmful bacteria on the skin, which can contribute to acne and other skin irritations.
- Soothing: Leuconostoc radish root ferment filtrate has been shown to have soothing properties, which can help to calm and reduce inflammation in the skin.

Moisturisation using 1% in cream compared to base cream without active.



Link: Data on file

#### PORPHYRIDIUM CRUENTUM EXTRACT (RED ALGAE EXTRACT)

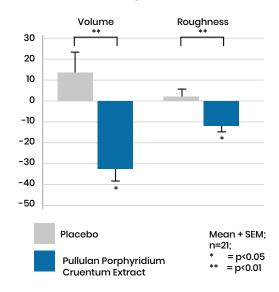
Ingredient Claims:

Protects the skin from the signs of ageing	Boosts moisture content in the skin
Helps to prevent the formation of wrinkles	Skin feels tighter and smoother

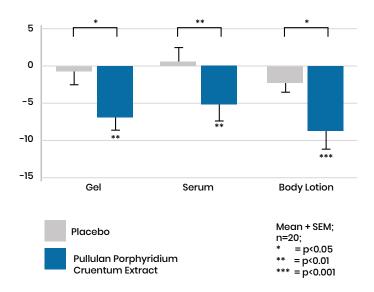
An extract derived from a type of red algae. Rich in vitamins, polysaccharides and lipids, Porphyridium cruentum extract possesses antioxidants such as phycoerythrin that help prevent the accumulation of free radicals in the skin can contribute to the formation of wrinkles. Porphyridium cruentum extract consequently helps to prevent the degradation of collagen and therefore wrinkle formation. Porphyridium cruentum extract also exhibits healing properties in addition to boosting the moisture content in the skin.

Porphyridium cruentum is a powerful extract that has been used in cosmetics as an antioxidant, anti-wrinkle agent, film former and moisturising agent. Over time it makes skin appear healthier, brighter, and reduces these visible signs of ageing.

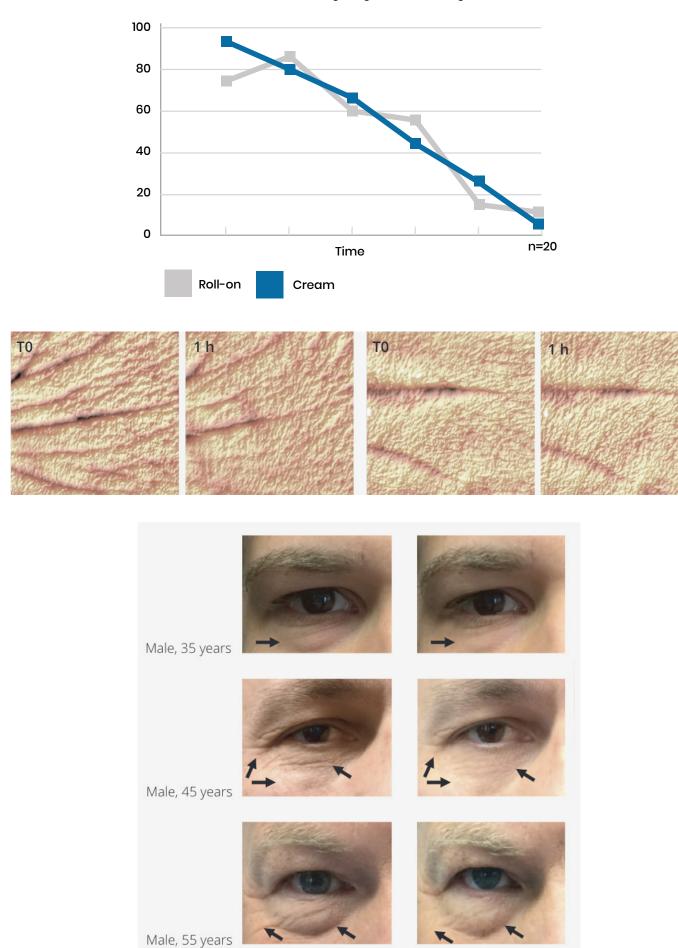
#### Wrinkle evolution compared to initial condition (%)



#### Skin roughness relative to initial condition (%)



**Testing Effect**% of volunteers feeling a significant tensing effect



before

after

Sources

Link: Data on file

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https://iopscience.iop.org/article/10.1088/1757-899X/980/1/012042/meta

https://www.mdpi.com/2079-9284/4/4/46

#### **PULLULAN (PULLULAN POLYSACCHARIDE)**

**Ingredient Claims:** 

Stimulates production of new collagen	Protects skin cells from oxidative damage
Skin feels smoother and tighter	Reduces the signs of ageing

A polysaccharide derived from a fungus that is beneficial in dermal regeneration and capable of stimulating fibroblasts to produce collagen. Pullulan also has antioxidant properties which can help to protect the skin from damage caused by free radicals. Free radicals are unstable molecules that can damage skin cells and contribute to the signs of aging. Pullulan forms a thin film on the surface of the skin, which can help to tighten and firm the skin. This can give the skin a smoother, more youthful appearance.

#### Sources

https://pubmed.ncbi.nlm.nih.gov/31350941/ https://pubmed.ncbi.nlm.nih.gov/31978478/