Unisooth EG-28
Rapid Control of Skin Irritation for the removal of Dark Circles

The appearance of dark circles is a biologically complex process closely linked to subocular micro-inflammation. By actively controlling this localized inflammation, Unisooth EG-28 acts on the 3 major causes of dark circles:

1) Reduction of skin inflammation
   › Decrease of redness, itching and pigmentation;

2) Stimulation of lymphatic circulation
   › Reduction of periorbital edema;

3) Vasorelaxation of under eye capillaries
   › Microcirculation improvement.
Focus on the product

Under eye dark circles are triggered by irritation

Dark Circles are the result of a complex set of biological parameters, that are closely linked to inflammation:

- Excessive pigmentation (accumulation of melanin)\textsuperscript{1,2} directly increases when skin is irritated.
- Periorbital edema\textsuperscript{2} becomes more visible when inflammation increases.
- Poor blood circulation\textsuperscript{3} causes the accumulation of non-oxygenated blood in capillaries and tissues due to blood leakage which increases the dark-bluish color of dark circles.

All of these processes increase upon aging and lead to darkening of the skin color under the eyes.

Unisooth EG-28: an optimized blend of “Gallate” derivatives...

Unisooth EG-28 is a balanced combination of activated forms of gallic acid which consists of the following:

- A glycosylated form of gallic acid coming from oak leaves
- A glycosylated form of epigallocatechin gallate originating from green tea
- Propyl Gallate

While propyl gallate is a well known lipoxygenase inhibitor and antioxidant in literature, gallic acid and epigallocatechin gallate inhibit histamine release, decrease cytokine production and reduce immune cell infiltration. The combination of these substances results in strong anti-inflammatory action coupled with significant antioxidant properties.

... to get rid of dark circles by decreasing under eye skin irritation

Unisooth EG-28 acts synergistically on several biological targets to block the initial causes of dark circle formation:

- It inhibits one of the major inflammation pathways of the body, NF-kB. This results in preventing the release of IL-8 and CXCL-1, two of the key cytokines involved in skin irritation and redness.
- It activates the pro-lymphatic factor VEGFR-3 gene expression to increase lymph circulation and reduce periorbital edema.
- It activates Heme Oxygenase 1 gene expression which is an anti-inflammatory and antioxidant factor. It is also well known to generate CO with vasorelaxant and endothelial cell protection effects. It assists in the recovery of normal blood flow under the eye and lessens blood leakage.

Clinical tests on 25 subjects have demonstrated a significant decrease of skin redness, water loss and appearance of dark circles as soon as 15 days!

Under eye dark circle

<table>
<thead>
<tr>
<th>Irritated darkened skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nf-kB activated: IL-8 and CXCL-1 released</td>
</tr>
<tr>
<td>Hyperpigmentation due to melanin production</td>
</tr>
<tr>
<td>Periorbital edema</td>
</tr>
<tr>
<td>Increased blood pressure</td>
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</tbody>
</table>

Normal under eye skin

<table>
<thead>
<tr>
<th>Soothed skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nf-kB inhibited, IL-8 and CXCL-1 release decreased</td>
</tr>
<tr>
<td>Melanin production diminished</td>
</tr>
<tr>
<td>Lymph circulation increase</td>
</tr>
<tr>
<td>Blood pressure decrease and increased blood flow circulation</td>
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</tbody>
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### Biological activity

#### Controlling key inflammation factors (*in vitro* tests)

Unisooth EG-28 was tested for its ability to inhibit the NF-kB pathway. Transformed human cells (HT29) were transfected with a NF-kB reporter gene plasmid. These were incubated for 24 hours with TNF-α in the presence or absence of Unisooth EG-28 at differing concentrations. A colorimetric reaction determined the NF-kB activity.

Unisooth EG-28 was tested for its ability to inhibit interleukin 8 (IL-8) and chemokine CXCL1 release in normal human epidermal keratinocytes (NHEK). The NHEK were incubated with TNF-α and interleukin-1α (both at 5 ng/ml, referred to as CTK mix).

Unisooth EG-28 was compared to the reference NF-kB Inhibitor III.

**Result:** Treatment with increasing doses of Unisooth EG-28 significantly inhibits up to -85% of the NF-kB activity in human cells induced with TNF-α.

*\(z>1.96\) Wilcoxon test

#### Promoting lymph circulation and vasorelaxation (*in vitro* tests)

Unisooth EG-28 was tested for its ability to stimulate the pro-lymphatic factor Vascular Endothelial Growth Factor Receptor 3 (VEGFR 3) and the Heme Oxygenase 1 gene expression. Human dermal microvascular endothelial cells were incubated for 24 hours in a medium containing or not containing Unisooth EG-28.

**Result:** 0.2% of Unisooth EG-28 increases VEGFR 3 (+675%) and Heme Oxygenase 1 (+194%) genes synthesis.
Clinical evaluation: reduction of skin inflammation...

Unisooth EG-28 was tested versus a placebo at 1% and 3% for its ability to reduce skin irritation. Skin irritation was induced by a 24h patch occlusion with a 2% sodium lauryl sulfate (SLS) aqueous solution on the skin. Erythema index (Mexameter®) and Trans-Epidermal Water Loss (Tewameter®) were evaluated after 15 min, 30 min, 60 min and 120 min.

Result: Unisooth EG-28 significantly reduces SLS-induced skin irritation compared to placebo. Redness was significantly decreased after 15 min (-8%) and up to -15% after 120 min, compared to placebo. TEWL (data not shown) was significantly decreased after 30 min (-17%) and up to -23% after 120 min, compared to placebo.

*p<0.05 compared to placebo, Student’s t Test

... Leading to a visible reduction of dark circles

A clinical trial was performed to evaluate the efficiency of Unisooth EG-28 on the reduction of dark circles. A gel containing 3% of Unisooth EG-28 was tested against a placebo in a double-blind study on 25 human volunteers. The products were applied twice per day for 30 days on the area around the eyes. Color changes of the dark circles were evaluated (spectrophotometer) after 15 and 30 days.

Result: Unisooth EG-28 significantly reduces dark circles compared to placebo in only 15 days with a visible reduction of under eye edema. There is a significant reduction of the Red (-21%) and the Blue (-21%) components after 30 days.
# Technical information

**INCI:** Water, Propyl Gallate, Gallyl Glucoside, Epigallocatechin Gallatyl Glucoside  
**Origin:** Glycosylated plant extract  
**Preservation:** Preserved with Benzyl Alcohol and Dehydroacetic Acid  
**Appearance:** Clear, yellow liquid  
**Solubility:** Water-soluble  
**Dosage:** 1 – 3%  
**Processing:** Can be added at the end of the formulation process under stirring or homogenizing. It can be heated for a short time with the water phase of a formulation. Formulate at pH between 5.0 and 7.0 and temperature below 40°C.

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## Claims

**Claims:** Removes under eye dark circles, anti puffiness, soothes instantly irritated skin, improves under eye microcirculation, protection from environmental stress.  
**Applications:** Eye contour, eye creams, eye serum, BB (Blemish Balm) creams, soothing treatments, protective care, sensitive skins, after sun / sun care products.
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