Densorphin™
For a dense, sexy and happy skin
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Stimulation of β-Endorphins and DHEA Activities to Redensify the Skin

Densorphin™ is a 100% natural active ingredient that is based on a concentrated extract of the monk’s pepper berries which stimulates the activities of β-endorphin and DHEA (Dehydroepiandrosterone). Densorphin™ is able to both effectively and rapidly redensify the mature skin of women and men.

As we grow older, the loss of sex hormones and β-endorphins affects the skin quality of both women and men.

DHEA (which is the precursor of sex hormones) and β-endorphins are interesting targets for cosmetic products as our skin is able to synthesize both of them locally and autonomously.

In vitro studies have demonstrated that Densorphin™ stimulates the biosynthesis of DHEA. Clinical studies performed on women and men aged over 50 years showed that Densorphin™ significantly increased the density and elasticity of their skin. In addition, before and after pictures clearly showed an anti-wrinkle effect.

Therefore, Densorphin™ reduces the andropause and menopause related loss in skin density and elasticity that is caused by hormonal changes in women and men aged over 50 years.

Densorphin™
• Increases the skin density after just one month
• Visibly fades away wrinkles
• Restores skin’s elasticity
• Builds cushion into time-thinned skin

Applications
• Anti-aging treatments for 50+
• Men’s skin care
• Collagen and elastin boosters
• Firming and lifting products
• Repair formulas

Formulating with Densorphin™
• Recommended use level: 2%
• Incorporation: For cold processes, dissolve Densorphin™ into the aqueous phase. In hot/cold processes, add during the cooling phase below 60°C.
• Thermostability: Temperatures of up to 60°C for a short time will not affect the stability of Densorphin™.

INCI (EU/PCPC) Declaration
Vitex Agnus Castus Extract / Vitex Agnus-Castus Fruit Extract (and) Maltodextrin (and) Aqua / Water

Additional Information
• Not preserved
• Alcohol-free
As We Age, the Levels of Certain Hormones Decrease

Hormones are signaling molecules that are produced by our body and permit the communication between organs and tissues. These messengers play an important role in physiology regulation and behavioral activities.

As we age, the levels of certain hormones decrease in both women and men. This is notably the case with regard to the sex hormones (estrogens and androgens), their precursor DHEA (Dehydroepiandrosterone) and β-endorphins, which are also known as the “happiness” hormone.

Hormonal Changes Affect the Skin Quality in both Women and Men

Both during and after the menopause / andropause, the skin undergoes many alterations which occur as a result of hormonal changes:

• In the epidermis, the cell turnover is reduced which leads to a thinning of the cutaneous tissue and a dehydration of the stratum corneum.
• In the dermis, the reduced synthesis in collagen (I and III) and hyaluronic acid caused by the loss in estrogens makes the skin lose its density and volume.

DHEA Contributes to Skin Density

DHEA derives from cholesterol and is produced in both women and men, mainly in the adrenal glands. From there, it is secreted in the general circulation. The adrenal secretion of DHEA increases progressively and reaches its maximum level around the age range of 20–30. From the age range of 40–50, it markedly decreases (1).

In several studies, the topical application of DHEA, was shown to induce collagen synthesis, decrease MMP levels (2) and increase skin thickness and hydration (3).

β-Endorphins Contribute to Skin Regeneration

β-endorphin is an analgesic (morphine-like) and euphoria-inducing molecule. It is mainly produced in the neurons of the central and peripheral nervous system. The word “endorphin” derives from the Greek words éndon, which means “from within” and Morpheús, who was the God of sleep in Greek mythology. These words together create “endo(genous) (mo)’rphine”.

β-endorphins accelerate wound healing and epithelialization. Furthermore, they stimulate fibroblast proliferation as well as the differentiation and migration of keratinocytes (6).

Changes in Andropausal and Menopausal Skin

<table>
<thead>
<tr>
<th>Young skin</th>
<th>Andropausal/menopausal skin</th>
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<tbody>
<tr>
<td>Decreased epidermal cell turnover</td>
<td></td>
</tr>
<tr>
<td>Reduced synthesis of collagen I and III</td>
<td></td>
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<tr>
<td>Reduced synthesis of hyaluronic acid</td>
<td></td>
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<tr>
<td>thinning of the cutaneous tissue</td>
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<tr>
<td>dehydration of the stratum corneum</td>
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<tr>
<td>loss of skin density and volume</td>
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DHEA and β-Endorphins
Two targets of interest for cosmetic products

DHEA and β-Endorphins are Linked Together
In the brain, DHEA exerts a protective effect on neurons thanks to its antioxidant and anti-inflammatory powers. In addition to this, DHEA modulates the synthesis and release of certain neurotransmitters such as dopamine and β-endorphins (4).

In women after menopause, whilst the β-endorphin levels are reduced, the oral administration of DHEA was shown to normalize these levels (5).

Our Skin Can Synthesize DHEA and β-Endorphins
It has recently been established that our skin holds all of the enzymes that are required for the synthesis of sex hormones either from circulating DHEA or even through the local conversion of cholesterol into DHEA (7). Therefore, our skin is able to autonomously control the intracellular level of sex hormones according to local needs.

Our skin is also able to produce the β-endorphin. Indeed, keratinocytes, fibroblasts and melanocytes are able to synthesize it independently of the central nervous system. Furthermore, these cells carry the specific receptor “μ-opioid receptor (MOR)” of this β-endorphin (6).

Consequently, these two molecules are extremely interesting targets for topically-applied products.

5. Genazzani et al., Fertility and sterility vol. 80, no. 6, December 2003
Densorphin™
Phyto-endorphins to redensify the skin

Monk’s Pepper Produces Substances with β-Endorphin Activity
Densorphin™ is based on a concentrated extract of monk’s pepper berries. Monk’s pepper (chaste tree, Vitex agnus-castus, Verbenaceae) is a deciduous shrub that is native to the Mediterranean region. Its black berries have been used since ancient times as a herbal medicine in order to treat inflammation, the spleen, premenstrual syndrome and injuries. It was recently discovered that compounds of monk’s pepper berries were able to bind to the MOR and exert a β-endorphin-like effect by activating them (8). For this reason, these natural molecules are called phyto-endorphins due to their ability to mimic the activity of β-endorphins.

Mechanism of Densorphin™
Densorphin™ stimulates the biosynthesis of DHEA and therefore enhances the skin’s ability to control the level of sex hormones. Furthermore, the active substance of Densorphin™ is known to have a β-endorphin-like effect.

Clinical studies that were performed on women and men aged over 50 years showed that Densorphin™ significantly increased the density of their skin in both the face and body regions of both genders. The elasticity of their skin was also significantly improved following treatment with Densorphin™. Finally, before and after pictures clearly showed an anti-wrinkle effect.

Therefore, Densorphin™ reduces the age-related loss in skin density and elasticity that is caused by hormonal changes in women and men aged over 50 years.
Densorphin™
Study results

Stimulation of DHEA Biosynthesis
The capacity of Densorphin™ to stimulate the formation of DHEA was evaluated in vitro against two reference substances that are known for their potency for influencing the sex hormones. Human adrenocortical cells (NCI-H295R) were either treated or not treated with different concentrations of the monk’s pepper berry extract. At the end of incubation, the morphology of the cells was controlled and the supernatants were collected for analysis. Secreted levels of DHEA and its product, androstenedione were analyzed by LC-MS. As reference items, the androgen suppressor ketoconazole and the DHEA inducer PP2, were used.

Results showed that the monk’s pepper berry extract was able to induce the biosynthesis of both DHEA and androstenedione in the cells in both a significant and dose-dependent way.

DHEA content was increased by 25% and 30% in the presence of 0.05% and 0.1% monk’s pepper berry extract respectively.

Androstenedione content was increased by 22% in the presence of 0.05% of monk’s pepper berry extract.
Densorphin™
Study results

Rapid Improvement in Skin Elasticity
Thirty volunteers (15 women and 15 men) aged between 52 and 76 years (mean age: 63.1 years) applied either a cream with 2% Densorphin™ or the corresponding placebo twice daily for a period of 28 days to the inner side of their forearms. The elasticity of their skin was determined by using a cutometer.

Results showed that Densorphin™ was able to rapidly increase the skin elasticity. Indeed, after 28 days of treatment, this parameter was increased by 7.1% compared to initial conditions and by an additional 3.8% compared to the placebo. The elasticity of the skin was increased for 77% of the volunteers.

Increase in Skin Elasticity

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>2% Densorphin™</th>
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<tbody>
<tr>
<td>After 14 days</td>
<td>0.6</td>
<td>4.0</td>
</tr>
<tr>
<td>After 28 days</td>
<td>2.2</td>
<td>6.8</td>
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*p<0.05 versus untreated
Densifying Effect on the Body in Just One Month

Thirty volunteers (15 women and 15 men) aged between 50 and 65 years (mean age: 57.7 years) applied either a cream with 2% Densorphin™ or the corresponding placebo twice daily for a period of 28 days to the inner side of their forearms. The density of their skin (epidermis + dermis) was determined by ultrasonic measurements.

The ultrasonic wave generates echoes when it is partially reflected at the boundaries between different tissue structures. The intensity of the reflected echoes can be evaluated and visualized in a color image. The collagen and elastic fiber structure of an intact dermis yields many reflections that are visible as bright colors in the ultrasonographic image. However, disruption to this regular architecture leads to weaker reflections and dark patches as can be seen in the ultrasonographic images below at Day 0. These so-called subepidermal low-echo-genic bands (SLEB) are commonly found in aged and photo-damaged skin.

Ultrasonographic images showed that Densorphin™ increased the density of the dermal tissue and this led to a visible reduction of the SLEB.

Treatment with Densorphin™ led to an average increase of skin density by 17.9% compared to initial conditions and by an additional 9.2% compared to the placebo.

Increase of Tissue Density – Body

![Graph showing increase in skin density in the body compared to initial conditions in %]

*\(p<0.05\) versus initial conditions and placebo
Densorphin™
Study results

Densifying Effect on the Face in Just One Month
Thirty volunteers (15 women and 15 men) aged between 50 and 65 years (mean age: 57.7 years) applied either a cream with 2% Densorphin™ or the corresponding placebo twice daily for a period of 28 days to their faces. The density of their skin (epidermis + dermis) was determined by ultrasonic measurements.

Ultrasonographic images showed that Densorphin™ increased the density of the dermal tissue and this led to a visible reduction of the SLEB.

Treatment with Densorphin™ led to an average increase of skin density by 4.4% compared to initial conditions and by an additional 4.8% compared to the placebo after just 28 days.

Increase of Tissue Density – Face

* p<0.05 versus initial conditions
Visible Anti-Wrinkle Effect

During the previously described study, high definition photographs were taken using the VisioFace®.

Results showed that after just 28 days of treatment with 2% Densorphin™, there was a visible reduction of the depth of wrinkles in the crow’s feet area.

Visible Reduction in Wrinkle Depth

Before

After 28 days
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• Repair formulas

Marketing Benefits
• Based on a Mediterranean plant that has β-endorphin-like activity
• Tested on both women and men
• Stimulation of DHEA levels
• Not preserved

Innovating for your success
Mibelle Biochemistry designs and develops innovative, high-quality actives based on naturally derived compounds and profound scientific know-how. Inspired by nature – Realized by science.

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