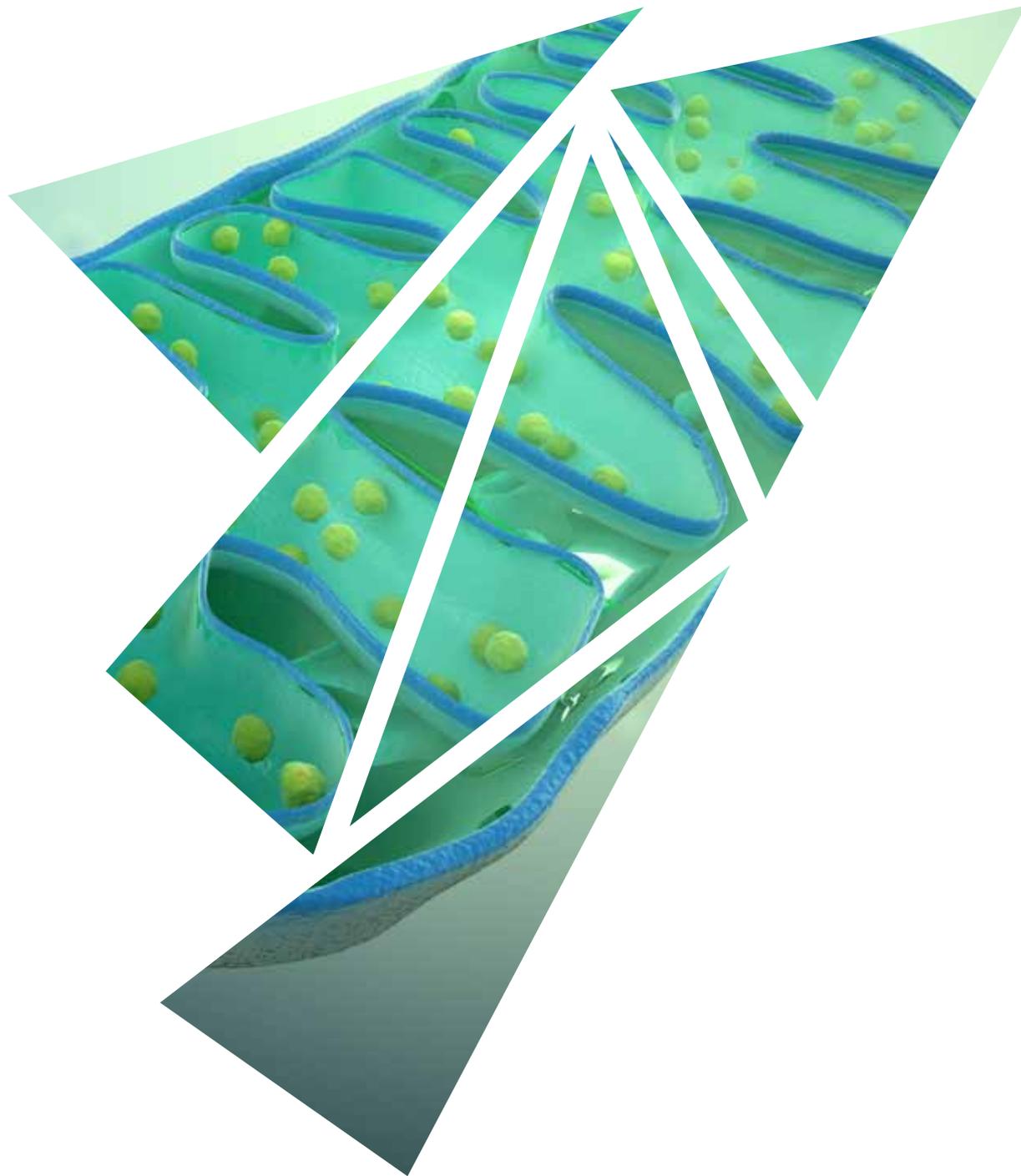


METHIOPEPTIDE[®]



CELL RESPIRATION RECOVERY

SKIN ENERGIZER

ANTI-AGING: « 2ND WIND » EFFECT

ANTI-STRESS: LONG LASTING PROTECTION

PHOTO-PROTECTION

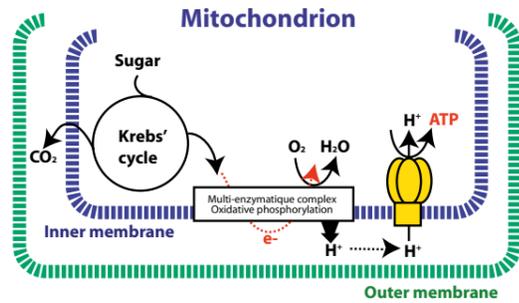
EXSYMOL
MONACO

METHIOPEPTIDE

AGING CELL RESPIRATION

Oxygen (O₂) is used by our organism to convert energetic molecules (sugars, aminoacids and lipids) into adenosine triphosphate (ATP), a versatile biochemical form of energy used to fuel metabolic processes. Cell respiration (O₂ consumption), occurs within mitochondria. These small cell sub-units can be considered as the cell's « powerhouses ».

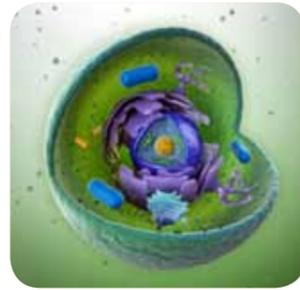
Cell respiration (oxidative phosphorylation) involves a multi-enzymatic complex located in mitochondria's inner membrane.



Oxygen (O₂) is the final acceptor molecule of electrons (e-) transferred within this complex, also called "respiratory chain". Electron transfer is coupled with proton (H⁺) exclusion from mitochondria inner compartment. Proton gradient enables ATP synthesis.

Mitochondria are vulnerable power plants

Many free radicals derived from oxygen (ROS) are formed within mitochondria either because of sunrays (UV or IR) or because of electron leakage from the respiratory chain.



The respiratory chain is damaged by ROS and this result in an increased electron leakage that also form ROS. All these ROS participate to skin premature aging.

Cell respiration declines with aging

With aging, the accumulation of non-repaired damages, due to ROS, results in a gradual impairment of the respiratory function (fewer ATP is produced). As a consequence, more and more electron leakage occurs, and ROS formation within the mitochondria is increased.



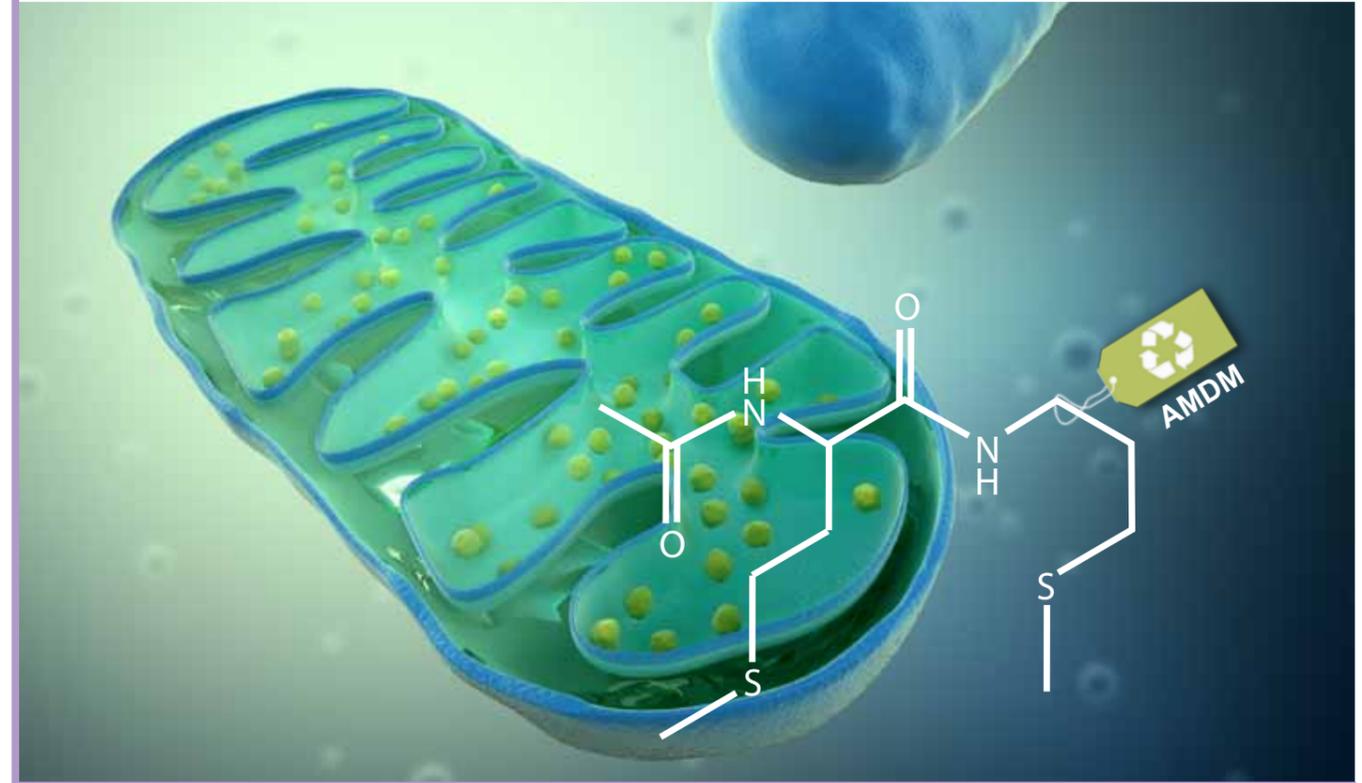
This respiration decline initiates a vicious circle: the energy production decrease weakens defense and repairing systems, which results in accelerated damages accumulation.

EXSYMOL 's SOLUTION:
a biobetter protector designed for recovery of the respiratory function

• **BIOMIMETIC:** METHIOPEPTIDE contains methionine, an antioxidant aminoacid present at high levels in mitochondrial proteins. METHIOPEPTIDE doesn't affect the oxidative phosphorylation process and is also recognized by MSR (Methionine Sulfoxide Reductase), an enzyme responsible for methionine recycling.

• **BIOBETTER:** METHIOPEPTIDE is much more effective than methionine.

METHIOPEPTIDE Applications



INCI name: METHYLTHIOPROPYLAMIDO ACETYL METHIONINE

METHIOPEPTIDE is a preservative-free 15% hydroglycolic solution of **AMDM** (Acetyl methionyl decarboxymethionine), a « biobetter » peptide derived from dimethionine.

- Inspired by skin natural defense
- Safe (no toxic end products)
- Recycled by skin enzymes (MSR)
- More efficient than natural methionine
- Bioavailable

Skin benefits

- Respiratory function recovery
- Mitochondria protection
- DNA protection
- Cell protection
- Photoprotection
- Intra-mitochondrial ROS scavenging

Cosmetic applications

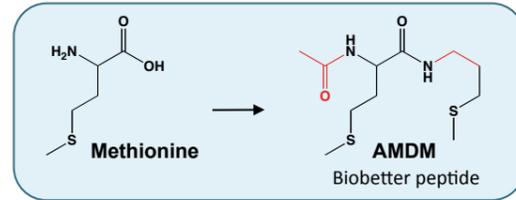
- Anti-aging
- Skin energizer: cell respiration protection
- Energy recycling
- Photo-protection
- Cells 2nd wind - Metabolic recovery
 - 1-Enhanced natural skin defense (epidermal survival)
 - 2-Optimized cell longevity
- Improved sun protection

METHIOPEPTIDE

Bio-better technology

GET INSPIRED BY NATURE AND EXCEED ITS POTENTIAL

Methionine is a versatile antioxidant amino acid that participates to proteins natural defense. It is known as the "last chance defense system", since it scavenges ROS when all other systems failed (antioxidant enzymes and antioxidant vitamins). Mitochondrial proteins, that are exposed to an important oxidative stress, are rich in methionine. **METHIOPEPTIDE** was designed for performance. Structural modifications improved its bioavailability (methionine penetration in skin and cells is low) and its reactivity towards ROS.



METHIOPEPTIDE is a biobetter

METHIOPEPTIDE is an improved methionine that is naturally present in all cells. It has a better resistance to enzymatic degradation (1), better cell penetration (2), a better skin penetration (3), and better scavenging abilities (4).

1 Resistance to hydrolytic enzymes

AMDM structural characteristics avoid **METHIOPEPTIDE** degradation in the superficial layers of the skin.

2 Penetration into skin cells (horizontal bio-availability)

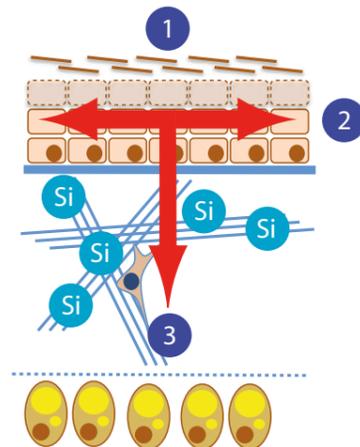
| | λ |
|---------------|-----------|
| Ac Methionine | 0.67 |
| AMDM | 2.03 |

3 Skin penetration (vertical bio-availability)

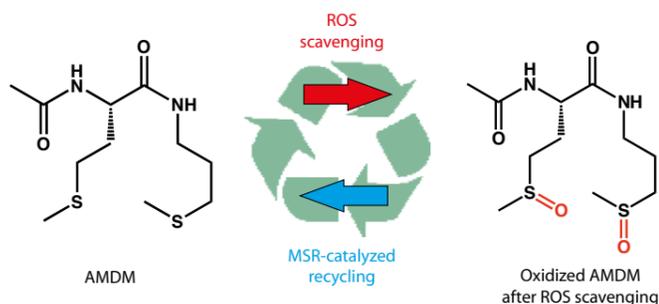
| | Log D (pH7) |
|---------------|-------------|
| Ac Methionine | - 4.65 |
| AMDM | 0.6 |

4 Scavenging of hydroxyl radicals (OH°)

| | OH° piégés à 30 mM |
|---------------|--------------------|
| Ac Methionine | 44% |
| AMDM | 83% |



Regeneration by MSR, an enzymatic recycling system



ROS-mediated oxidation of methionine is reversible. Indeed, oxidized methionines within proteins are reduced into native methionines by the action of Methionine Sulfoxide Reductase (MSR), an enzyme naturally present in the skin. Thanks to AMDM close resemblance with methionine, the oxidized forms of AMDM can be recognized and regenerated by MSR. Hence, **METHIOPEPTIDE** can provide the skin with a long lasting protection.

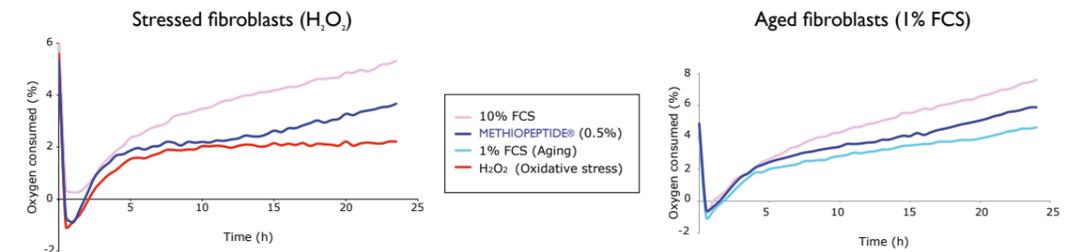
METHIOPEPTIDE

Optimized cell respiration

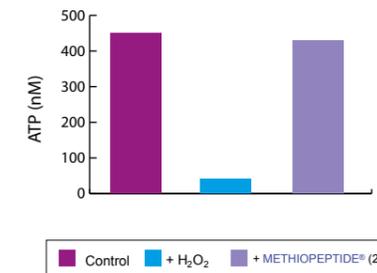
Oxygen is essential for life, and almost all of it is used to produce energy (ATP synthesis in the respiratory chain). As a consequence, oxygen consumption monitoring (oxymetry) is an accurate method to determine cell health, and cell response to stress (ROS, pollutants, UV).

In vitro oxymetry test

With age, or because of a stress, the cell respiration process is affected. As a result, fewer energy (ATP) will be produced. **METHIOPEPTIDE** (0,5%) is capable of protecting the cell respiration from aging and from the noxious effects of an oxidative stress.

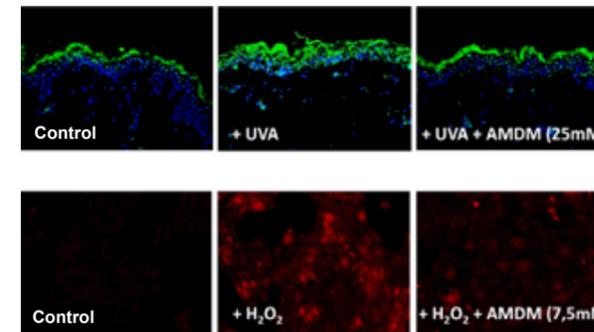


A protected energy synthesis



In the case of an H₂O₂-induced oxidative stress, cell oxygen consumption decreases leading to a decrease of ATP production. **METHIOPEPTIDE** (2%) managed to maintain an optimal energy level.

Mitochondria protection



Mitochondria are responsible for supplying the cells with energy. These organelles are vulnerable to stress. It is therefore of primary importance to protect them from harm. Exposure to UV rays leads to an intra-mitochondrial ROS overproduction (green). **METHIOPEPTIDE** (5%) is capable of reducing this UV-induced ROS production.

When mitochondria are exposed to this oxidative stress they are damaged (damaged mitochondria marked in red) and/or destroyed. **METHIOPEPTIDE** (1.5%) is able to protect mitochondria from oxidative stress. By protecting mitochondria, **METHIOPEPTIDE** contributes to an optimal energy supply for the skin.

Skin benefits of a rejuvenated cell respiration

With an energetic increase of cell metabolism, skin will benefit of high level of protection and health.

Global protection

METHIOPEPTIDE is capable of protecting skin cells at all levels:

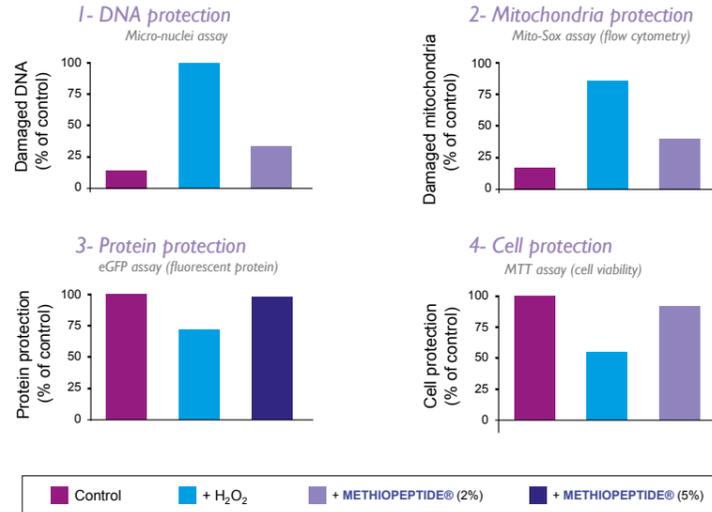
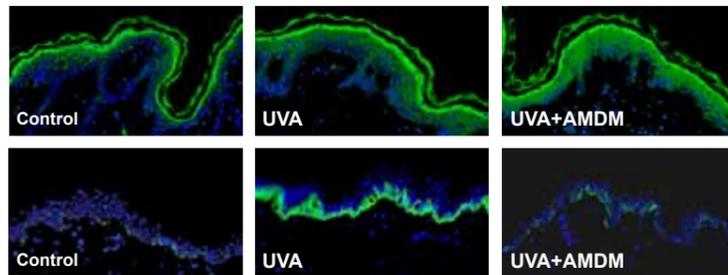


Photo-protection

Because of sunrays exposure, a few reactions in the skin that are responsible for the weakening of natural defenses may happen.



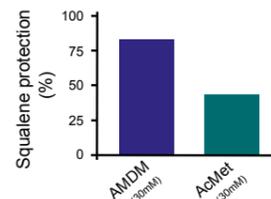
METHIOPEPTIDE is able to prevent the apparition of oxidized tyrosine (marked in green) and there for to maintain optimal defense mechanisms for the skin. Because the skin cells are better protected, the number of dying cells (marked in green) is substantially decreased in the case of a treatment with METHIOPEPTIDE.

Sun care – special feature

Many studies have shown that, in order to ease the free radical quenching, there is an overproduction of MSR, the enzyme responsible for the recycling of methionine sulfoxide back into methionine. Since MSR is also able to recycle AMDM, an increased quantity of MSR also means a higher quantity of AMDM available for the skin to use as a photoprotector.

Prevention of greasy skin - Anti-comedogenic

Squalenes are the first lipids on skin surface that suffer from radiation-induced oxidation. Once oxidized, they become toxic, create an inflammation and form comedones (blackheads). AMDM protects these squalenes and therefore the skin quality.



ANALYTICAL COMPOSITION

| | |
|-------------------------|-----|
| AMDM | 5% |
| Methylpropanediol | 50% |
| Water..... | 45% |

PHYSICO-CHEMICAL CHARACTERISTICS

Limpid and colorless liquid.
pH ≈ 5.5.
Miscible with water, alcohol and glycol.

PRESERVATIVES

No preservative.

TOLERANCE & TOXICITY STUDIES

METHIOPEPTIDE is perfectly tolerated. Tolerance and toxicity studies were performed using both *in vitro* (cell culture and reconstructed epidermis) and *in vivo* (human volunteers) methods.

FORMULATION

Advised doses: 2%.
Store at room temperature.

AVAILABILITIES

Available in 1, 5 and 30 kg drums.

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