METHIOPEPTIDE®

Cell respiration recovery
Skin energizer
Anti-aging: « 2nd wind » effect
Anti-stress: long lasting protection
Photo-protection
Cell respiration (oxidative phosphorylation) involves a multi-enzymatic complex located in mitochondria’s inner membrane. Oxygen ($O_2$) 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**

**Bio-better technology**

**GET INSPIRED BY NATURE AND EXCEED ITS POTENTIAL**

Methionine is a versatile antioxidant aminoacid 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 bio-better**

**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)**
   - Ac Methionine: 0.67
   - AMDM: 2.03

3. **Skin penetration (vertical bio-availability)**
   - 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 Sulfone 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.

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

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.

METHIOPEPTIDE is capable of protecting skin cells at all levels:

1. DNA protection
   MethPDH assay (fluorometric assay)
   
2. Mitochondria protection
   Mito-Sox assay (fluorometric assay)
   
3. Protein protection
   eGFP assay (fluorescent protein)
   
4. Cell protection
   MTT assay (cell viability)
   
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.

Photo-protection

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.

Prevention of greasy skin - Anti-comedogenic

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