Ergothioneine

- A Stable, Safe, and Powerful Natural Antioxidant -

NAGASE & CO. uses fermentation techniques to produce the natural antioxidant ergothioneine (Figure 1). A safe and stable compound, ergothioneine is transported to the brain and throughout the body.

What is Ergothioneine?

A rare amino acid, ergothioneine (EGT) is a natural compound with excellent antioxidant properties. Certain mushrooms (in the class basidiomycetes), fungi such as *Aspergillus oryzae*, *Streptomyces* species, and cyanobacteria are the only organisms capable of producing EGT. Humans must therefore eat mushrooms or foods fermented by *A. oryzae* to obtain EGT. EGT, discovered in 1909 [1], has been known for many years but has attracted attention for its fascinating properties only recently.

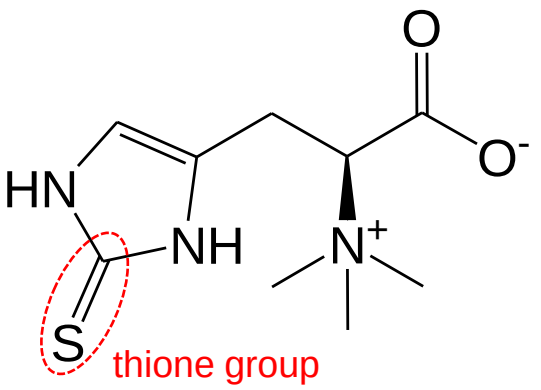

Figure 1. L-ergothioneine (EGT)

1. EGT Has Excellent Antioxidant Properties

A superior antioxidant, EGT eliminates reactive oxygen species 3 to 30 times better than glutathione [2], which is the most common significant antioxidant in the body . The activity is dependent on the type of reactive oxygen species. The powerful antioxidant properties of EGT are due to a special structural element called a thione group (Figure 1). Many antioxidants are unstable in the presence of molecular oxygen. However, by virtue of its thione group, EGT is not degraded in water for long term due to very low reactivity with oxygen, although EGT reacts rapidly with reactive oxygen species such as hydroxyl radical and singlet oxygen. EGT is also very stable in heat or acidic environments [3] and is very safe, showing no toxicity in humans [4].

2. Discovery of the Ergothioneine Transporter

EGT has recently attracted attention primarily because of a 2005 discovery that humans have an ergothioneine transporter that moves EGT into cells in the body [5]. Plants, fish, mammals, and many other forms of life have also been shown to use this transporter even though EGT is produced by only a few microorganisms. The ergothioneine transporter is expressed in many human tissues, where it imports EGT in high concentrations to protect cells from forms of oxidative stress [3], as follows.

i. Mitochondria are vital organelles that use oxygen to produce energy in the form of ATP. However, their reliance on oxygen leaves them vulnerable to oxidative stress. Poor mitochondrial function causes aging and many diseases. Researchers found that the ergothioneine transporter is heavily expressed in the mitochondrial membrane [6].

ii. Red blood cells, the body's oxygen distributors, express higher amounts of the ergothioneine transporter than almost any other type of cell in the body. Not surprisingly, EGT is found in high concentrations in red blood cells (about 2 mM) [7].

iii. The ergothioneine transporter is also expressed in the skin and especially so in cells on the epidermal side, where EGT is found in high concentrations [8]. It is believed that epidermal cells accumulate high levels of EGT to protect them from oxidative stress caused by ultraviolet light.

iv. Despite its high solubility in water, EGT crosses the blood-brain barrier. The compound is found in tissues of the central nervous system. Multiple studies have shown EGT to be effective in treating neurodegenerative diseases, which are often the result of oxidative stress [9, 10].

It is fascinating from a physiological standpoint that the ergothioneine transporter is highly expressed in cells and organelles susceptible to oxidative stress and that these cells can import this powerful antioxidant.

3. EGT Induces Stem Cell Differentiation

Recent studies have shown that EGT helps induce stem cells to differentiate. For example, exposing nerve stem cells to EGT induces them to differentiate into neurons. This finding suggests that dietary EGT could help nerve cells to regenerate following nerve damage [10,11].

Potential Effects of Ergothioneine

EGT may inhibit neurodegenerative diseases (e.g., Alzheimer's disease, Parkinson's disease), depression, UV-induced skin aging (wrinkles and blotches), cataracts, and glycative stress. Accumulated levels of EGT in the body's cells, however, decrease with age [9]. Regularly consuming EGT may therefore suppress various age-related diseases.

NAGASE's Ergothioneine-Production Technologies

As stated above, EGT is a highly attractive compound, but applying the potential benefits of EGT to human health has long been hampered by an inability to inexpensively and consistently mass-produce EGT with existing techniques, such as by extraction from mushrooms. To correct this, NAGASE is developing a novel fermentation process to produce ergothioneine from inexpensive saccharides using NAGASE's N-STePP®, a *Streptomyces*-based technology that has generated considerable interest in the biotechnology field [12].

References

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The NAGASE R&D Center is committed to developing processes for efficiently producing a wide range of compounds with proprietary fermentation technologies. Click on the following link to learn more about research partnerships with commercial applications (e.g., industrial process development, and the evaluation and exploration of various applications of lab samples).

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