

Mechanism and Clinical Study of Ergothioneine from Golden Oyster Mushroom on Anti - Aging Effects of Human Skin and Cells

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Abstract: Aging is a natural phenomenon in the process of life, which is not only a research focus of modern medicine, but also a long-term topic of exploration in cell biology. Cell biology believes that aging is a process of cellular function degradation over time, which is influenced by multiple factors and mainly involves the following core mechanisms: cell apoptosis and failure, decreased mitochondrial function, shortened cell telomeres, and chronic low-grade inflammation. These mechanisms interweave with each other, gradually leading to "aging manifestations" such as skin laxity, cognitive decline, and metabolic decline. Golden Oyster Mushroom (*Pleurotus citrinopileatus* Sing.), as a natural fungus with both medicinal and edible values, its active ingredient ergothioneine has been confirmed by modern research to have significant antioxidant, anti - glycation and skin aging - delaying effects. Based on the theory of "human aging originates from cell aging" in cell biology, combined with the 28 - day randomized double - blind clinical trial data of GOM - HCER® ergothioneine from Golden Oyster Mushroom, this study systematically explores its anti - aging effect. The test results show that continuous daily intake of 100mg GOM - HCER® can effectively improve the skin gloss (increased by 3.638%), elasticity (increased by 5.357%), water content (increased by 7.599%) and reduce the wrinkle area (decreased by 21.071%) of the subjects, and show significant advantages over the placebo group in anti - glycation reaction. Based on the theory of cell biology research, this experimental study believes that ergothioneine contained in GOM-HCER® can delay skin aging through cell biological processes such as mitochondrial function protection, DNA repair, inflammatory aging regulation, and Sirtuin pathway activation.

Keywords: Golden Oyster Mushroom; Ergothioneine; Mitochondria; Cell Anti - Aging; Anti - Aging; Skin Health; Anti - Glycation

1. Introduction

Aging, as a natural physiological phenomenon, is not merely a change in appearance; it also reflects the gradual decline in the functions of multiple bodily systems. At the cellular level, aging is closely associated with factors such as oxidative damage, inflammatory responses, and the accumulation of glycation products. These physiological changes gradually lead to the decline of various bodily systems. Modern medical research typically focuses on these molecular and cellular-level alterations, aiming to uncover the underlying mechanisms of aging [1-2]. However, aging is not merely the decline of individual cells or organs; it involves comprehensive changes across the entire body. Therefore, understanding aging requires a more systematic and comprehensive perspective [3].

Among the many directions of anti - aging research, the role of natural medicines has increasingly become the focus of attention. Golden Oyster Mushroom (*Pleurotus citrinopileatus* Sing.) is a fungus with both medicinal and edible values widely used in Asia. It is not only used as a food ingredient but also its rich bioactive components have attracted much attention. Among them, ergothioneine is a component with strong antioxidant and anti - glycation properties, which is considered to have significant anti - aging potential. Studies have shown that ergothioneine can effectively slow down the aging process and improve skin aging symptoms by scavenging free radicals, reducing oxidative stress, and inhibiting the accumulation of glycosylation products [4 - 5].

This study aims to explore the mechanism and clinical application effect of ergothioneine from Golden Oyster Mushroom (*Pleurotus citrinopileatus* Sing.) on skin aging through theoretical research of modern cell biology. Through a 28 - day double - blind clinical trial, the actual effect in anti - aging is

verified, providing a theoretical basis and practical guidance for modern clinical medicine and anti - aging product development. On this basis, it is hoped to provide new insights for the research on aging mechanisms and the innovation of anti - aging therapies, and provide effective solutions for the increasingly concerned health and beauty needs of modern society.

2. Theoretical Analysis of the Essence of Human Aging in Cell Biology Research

2.1 Mitochondrial Dysfunction

Mitochondrial dysfunction is one of the core mechanisms driving human cell aging. With age, the energy production efficiency of mitochondria gradually decreases, and the function of the electron transport chain (ETC) weakens, resulting in a reduction in ATP production and more leakage of reactive oxygen species (ROS). Excessive ROS will attack mitochondrial DNA (mtDNA), causing the accumulation of mutations, further damaging the function of ETC, and forming a vicious circle. In addition, the mitochondrial dynamic balance of senescent cells is disturbed - excessive division and insufficient fusion lead to the accumulation of fragmented mitochondria, while the damaged mitophagy system cannot effectively remove these dysfunctional mitochondria. At the same time, the decrease in NAD⁺ level leads to the reduction of deacetylase SIRT activity, affecting metabolic regulation and DNA repair, and accelerating cell function decline. Therefore, mitochondrial dysfunction ultimately promotes cells to enter a senescent state.

In this theoretical framework, ergothioneine (EGT) contained in GOM-HCEr®, as a natural antioxidant, can effectively improve mitochondrial dysfunction. Its unique sulfhydryl structure can selectively scavenge reactive oxygen species (ROS) in mitochondria, reduce oxidative damage, and protect the integrity of mitochondrial DNA (mtDNA) and electron transport chain (ETC) proteins. At the same time, EGT enhances cellular antioxidant defense capacity by regulating the Nrf2/ARE pathway, inhibits the decrease of mitochondrial membrane potential, and maintains efficient ATP synthesis. In addition, EGT can reduce the release of inflammatory factors and block the vicious circle between ROS and inflammation, thereby delaying cell aging related to mitochondrial dysfunction. Studies have shown that EGT shows significant mitochondrial protective effects in neurodegenerative diseases and aging models [6].

2.2 Theory of Telomere Shortening

Telomere shortening is also one of the important reasons for cell aging. Telomeres are repeated DNA sequences (TTAGGG) located at the ends of chromosomes. Their length gradually shortens with cell division, which is due to the inability of DNA polymerase to completely replicate the ends of linear chromosomes (the "end replication problem"). When telomeres shorten to a critical length, they will trigger a DNA damage response, induce cell cycle arrest through the p53 - p21 pathway, and make cells enter an irreversible senescent state (replicative senescence). In addition, excessively short telomeres can lead to chromosome end fusion and genomic instability, further aggravating cell dysfunction. The lack of telomerase (TERT) activity in most somatic cells accelerates this process, while the reactivation of telomerase activity may prolong cell life. Studies have shown that telomere shortening is closely related to a variety of age - related diseases (such as atherosclerosis, fibrosis) and the overall aging phenotype [7].

Ergothioneine (EGT) in GOM-HCEr® can selectively scavenge reactive oxygen species (ROS) in mitochondria and nuclei, reduce oxidative stress damage to telomere DNA (rich in guanine, vulnerable to oxidative attack), thereby delaying telomere erosion. At the same time, EGT enhances the endogenous antioxidant defense system in cells (such as superoxide dismutase and glutathione) by activating the Nrf2 pathway, and indirectly maintains telomere stability. In addition, EGT can inhibit the activation of pro - inflammatory factors (such as NF - κB) and block the mechanism of accelerating telomere wear related to inflammation. Studies have shown that EGT can prevent abnormal telomere fusion by maintaining the function of telomere - binding proteins (such as TRF2), thereby protecting genomic integrity [8].

2.3 Persistent Chronic Low - Grade Inflammation

Chronic inflammation is also an important driving factor of aging. It leads to tissue damage and functional decline by continuously activating the immune system. With age, the imbalance of the immune system (such as excessive activation of inflammasomes and increased release of pro - inflammatory

factors) forms an "inflamm - aging" state. This low - grade chronic inflammation will accelerate cell aging, inhibit stem cell function, and promote oxidative stress and mitochondrial dysfunction. At the same time, inflammatory mediators (such as IL - 6, TNF - α) can damage telomere stability, induce DNA damage, and aggravate age - related diseases (such as atherosclerosis, neurodegenerative diseases) by activating pathways such as NF - κ B. Studies have also found that chronic inflammation and the accumulation of senescent cells form a vicious circle, further promoting the decline of organ function and the overall aging process.

Ergothioneine contained in GOM-HCEr® can alleviate chronic inflammation through multiple mechanisms to delay aging. Its unique sulfhydryl structure can efficiently scavenge reactive oxygen species (ROS), inhibit the activation of NF - κ B and NLRP3 inflammasomes induced by oxidative stress, and reduce the release of pro - inflammatory factors such as IL - 1 β and TNF - α . At the same time, EGT enhances cellular antioxidant defense capacity by regulating SIRT1 and Nrf2 pathways, protects mitochondrial function, and reduces inflammation - related cellular senescence. In addition, it can inhibit the production of senescence - associated secretory phenotype (SASP), block the vicious circle between inflammation and aging, thereby reducing tissue damage and delaying age - related functional decline. [9 - 11]

GOM-HCEr®, as a natural ingredient rich in ergothioneine, has multi - dimensional mechanisms in skin anti - aging through clinical verification, including anti - oxidation, anti - glycation, and promotion of blood circulation [12]. These mechanisms not only help delay skin aging but also enhance the body's self - repair and immune capacity. Integrating the biological theory that "aging is the external manifestation of the body's cellular state" can provide a more comprehensive and in - depth explanation framework for modern skin care and aging research [13].

3. Research Methods

This study combines the relevant theories of cell biology to analyze the mechanism of improving skin condition at the cellular level, and specifically discusses how to promote skin health by improving mitochondrial function, avoiding telomere shortening, and improving chronic inflammation. The study will analyze the correlation between the changes in skin condition before and after the test and these theories, aiming to reveal its potential mechanism in improving skin condition.

After the test, the skin condition of all subjects will be analyzed using cytological theories, focusing on whether these interventions are closely related to the improvement of skin gloss, elasticity, water content, and wrinkles.

3.1 Trial Design

This study employs a double-blind, randomized controlled clinical trial design to evaluate the efficacy of GOM-HCEr® (Golden Oyster Mushroom extract) in improving skin condition. The trial duration is 28 days, with 26 healthy participants aged 30 to 48 years old recruited (4 males and 22 females). All participants underwent a health screening prior to enrollment to ensure they had no skin diseases or other conditions that could affect skin condition. Before the trial began, participants were randomly assigned to either the experimental group or the control group. The experimental group received 100 mg of GOM-HCEr® orally daily, while the control group received 100 mg of placebo orally daily. All participants underwent skin condition assessments and evaluations at the start of the trial, on day 14, and on day 28.

The inclusion criteria for this study were: age between 30 and 48 years, no restrictions on gender, no history of skin diseases or other systemic conditions affecting skin condition, no history of allergies, no prior use of similar skin care products, and exclusion of pregnant or breastfeeding women.

All eligible participants signed an informed consent form prior to the trial to ensure they understood the purpose, process, potential risks, and rights of participants. Participants were randomly assigned to either the experimental group (GOM-HCEr®, 100 mg/day) or the control group (placebo, 100 mg/day). Each group consisted of 13 participants.

3.2 Testing Items and Instruments

To comprehensively assess skin condition, standardized instruments were used to measure various skin parameters, as shown in Table 1:

Table 1 Testing Items and Instruments

Indicator	Detection Instrument
Skin Glossiness	Glossymeter GL200
Skin Elasticity	Cutometer dual MPA580
Skin Moisturization	MDD4- Corneometer CM825
Skin Wrinkles	VISIA Skin Analysis
Advanced Glycation End-products (AGEs)	Fluorescence Quantitative Microplate Reader (370nm/440nm)

The skin gloss tester probe is shown in Figure 1.



Figure 1 Glossymeter GL200

The skin elasticity tester is shown in Figure 2.



Figure 2 Cutometer dual MPA580

The skin moisture tester is shown in Figure 3.



Figure 3 MDD4- Corneometer CM825

The skin wrinkle detector is shown in Figure 4.



Figure 4 VISIA Skin Analysis

3.3 Experimental Process

The entire process of this study strictly followed standardized experimental procedures, managed throughout by experienced researchers to ensure the scientific rigor, rigor, and reproducibility of the results. The trial was conducted at a certified clinical trial center equipped with the necessary facilities and qualifications, and provided strict quality control to ensure the stability of the experimental environment and conditions.

Prior to the trial, all participants underwent detailed health assessments and skin condition examinations. Preliminary screening utilized a series of standardized skin assessment tools to ensure that each participant had no significant differences in skin condition prior to the trial and no underlying health issues that could influence the trial results. Basic health information, including age, weight, and allergy history, was recorded for all participants. Additionally, all participants were informed of the trial details and signed informed consent forms to ensure their voluntary participation and informed consent.

During the actual trial, all participants will undergo skin condition assessments on Day 0 (pre-trial), Day 14, and Day 28. During each assessment, researchers will use high-precision instruments to collect data, with assessment indicators including skin luster, elasticity, hydration, wrinkles, and advanced glycation end products (AGEs). All assessment results will be recorded through a standardized process to ensure data accuracy.

During the trial, participants will consume the trial samples daily as specified. Researchers will distribute samples to each participant at the start of the trial and monitor compliance through regular follow-ups to ensure strict adherence to the prescribed schedule and dosage. To avoid bias or interference with trial results, participants will not be informed of the type of trial sample they are consuming (double-blind design). Additionally, the appearance and taste characteristics of the samples in the experimental group and control group were designed to be similar, further ensuring the implementation of the blinded design.

To ensure that participants could maintain their daily living habits during the trial and minimize the influence of external factors on skin condition, researchers required participants to avoid using any other topical products that might interfere with skin condition during the trial, including but not limited to skincare products, ointments, and other health supplements. Additionally, all participants were instructed not to alter their daily diet or lifestyle habits (such as sleep schedules and exercise levels) during the trial period to enable a comprehensive assessment of the independent effects of GOM-HCEr® on skin condition.

3.4 Intervention Measures for the Experimental and Control Groups

In this study, participants were randomly assigned to two groups: the experimental group and the control group. Participants in each group strictly followed the same trial protocol to ensure the reliability and fairness of the trial results.

Experimental Group: Participants in this group took 100 mg of GOM-HCEr® (Golden Oyster Mushroom extract) orally daily for 28 days. GOM-HCEr® is a natural extract containing ergothioneine, which is known to have potential bioactive properties in antioxidant and anti-glycation effects. Participants in the experimental group took a fixed dose of GOM-HCEr® daily and underwent regular skin assessments to evaluate improvements in skin radiance, elasticity, hydration, wrinkles, and anti-glycation effects.

Control group: Participants in this group took 100 mg of placebo daily for 28 days. A placebo is an inert substance without active ingredients, typically used in control groups to assess the impact of other

potential factors on skin condition. Participants in the control group maintained consistent lifestyle habits, diet, and external skincare product usage with those in the experimental group during the trial period, with the sole difference being the type of substance ingested, ensuring statistically significant comparison results between the two groups.

During the trial, all participants were required to strictly adhere to guidelines regarding lifestyle habits. Specifically, participants were instructed to maintain regular sleep schedules, healthy dietary habits, and avoid any external factors that could potentially affect skin condition, such as the use of non-recommended topical skincare products. By doing so, researchers could minimize confounding variables during the experimental process, ensuring both internal and external validity of the trial.

Additionally, to further ensure the rigor of the trial, all samples, medications, and placebos were carefully designed in terms of packaging, appearance, and taste, making it impossible for participants to distinguish between GOM-HCEr® and the placebo. The implementation of this double-blind design effectively prevented participant bias or expectations from influencing the trial results, ensuring the objectivity and accuracy of the data.

3.5 Data Collection and Analysis Methods

All skin condition data were collected using standardized instruments at various stages of the trial and processed using statistical analysis software. Researchers conducted data analysis through the following steps:

Descriptive Statistics: Descriptive statistics were performed on the participants' basic characteristics and skin metric data, calculating the mean and standard deviation of each metric.

Comparative Analysis: Paired t-tests were used to analyze changes in skin metrics between the experimental and control groups at different time points. To verify whether differences between groups were statistically significant, one-way analysis of variance (ANOVA) was employed.

Correlation analysis: Correlation analysis was performed between changes in skin metrics and factors such as the subjects' health status and age to explore the impact of different factors on skin improvement.

Glycation analysis: Fluorescence intensity analysis was conducted to assess changes in AGEs levels, and the anti-glycation effects between the two groups of subjects were compared.

4. Results and Discussion

4.1 Improved Skin Luster

Skin luster is an important indicator for assessing skin youthfulness and overall health. Using the Glossmeter GL200 gloss measurement probe, the average skin luster of the GOM-HCEr® group increased from 39.58 ± 6.23 before the trial to 41.02 ± 8.59 on day 28, representing an increase of 3.638%. The control group showed no significant changes, suggesting that the Golden Oyster Mushroom extract has a role in improving skin dullness and enhancing skin radiance.

4.2 Enhanced Skin Elasticity

Skin elasticity was measured using the Cutometer dual MPA580 skin elasticity tester. The GOM-HCEr® group showed an increase from 0.56 ± 0.05 to 0.59 ± 0.06 , representing a 5.357% improvement. Enhanced elasticity helps resist gravitational forces and facial expressions, thereby delaying wrinkle formation.

4.3 Enhanced Skin Moisturization

Using the MDD4-Corneometer CM825 moisture tester, the skin moisture index of the GOM-HCEr® group increased from 54.58 ± 8.52 to 58.62 ± 8.18 , representing a 7.599% increase. Increased moisture content effectively improves dryness and roughness associated with aging, providing the skin with a foundational “moisturizing environment.”

4.4 Significant Reduction in Wrinkle Area



Figure 5 Comparison of Skin Wrinkles

Using the VISIA skin imaging analysis system, the wrinkle values of the test subjects decreased from 8.59 ± 5.04 before the trial to 6.78 ± 4.56 on day 28, a reduction of 21.071%. This data indicates that GOM-HCEr® has significant efficacy in slowing down skin aging patterns and enhancing skin firmness. Compare the pictures as shown in Figure 5.

The results of various skin tests are shown in Table 2.

Table 2 Skin data indicators at different testing stages

Skin Condition	Pre-Test	Day 14	Day 28
Skin Glossiness	39.58 ± 6.23	40.24 ± 7.58	41.02 ± 8.59
Skin Elasticity	0.56 ± 0.05	0.57 ± 0.05	0.59 ± 0.06
Skin Moisture	54.58 ± 8.52	56.97 ± 8.24	58.62 ± 8.18
Skin Sensitivity	8.59 ± 5.04	7.64 ± 5.44	6.78 ± 4.56

4.5 Outstanding anti-glycation effects

The trial also assessed the performance of ergothioneine in anti-glycation. The primary causes of skin aging in humans include sun exposure, oxidation, and glycation. Glycation refers to non-enzymatic glycation reactions, where under non-enzymatic conditions, the free amino groups of macromolecules such as proteins, amino acids, lipids, or nucleic acids react with the carbonyl groups of reducing sugars through a series of reactions including condensation, rearrangement, cleavage, and oxidative modification, ultimately forming advanced glycation end products (AGEs). AGEs are closely associated with skin aging. Excessive AGEs can undergo glycation cross-linking reactions with skin elastic fibers and collagen, and since AGEs are brown in color, they ultimately cause skin yellowing and reduced elasticity.

Conventional AGEs exhibit fluorescent properties. Modeling can be performed based on the principle that glucose undergoes glycation reactions with human serum proteins to form AGEs. After oral administration of anti-glycation samples, their inhibitory effects on AGEs can be evaluated using fluorescent quantitative methods to assess their anti-glycation efficacy.

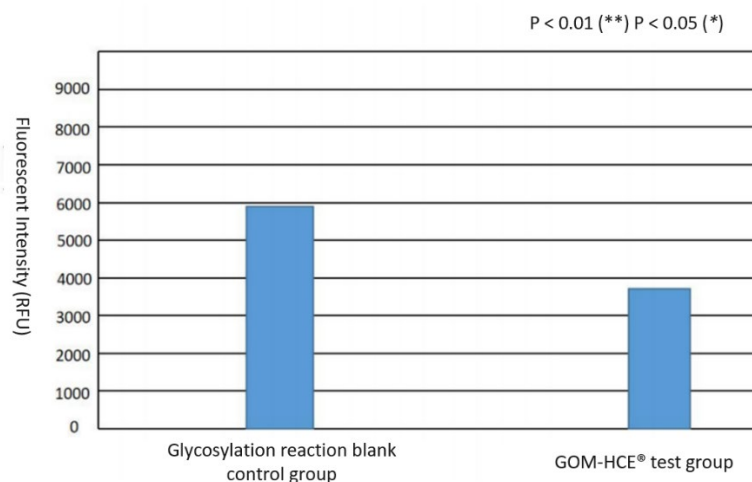


Figure 6 Anti-glycation reaction results

Skin stratum corneum samples were collected from participants using a stratum corneum sampling

strip. The samples were then incubated at 60°C for a specific duration and analyzed using a fluorometer under fluorescence detection conditions at 370 nm/440 nm to measure changes in AGEs levels, thereby assessing whether the test samples possess anti-glycation efficacy. In the study, stratum corneum sampling strips were used to extract samples, and AGEs (advanced glycation end-products) levels were detected using a fluorescence microplate reader at 370 nm/440 nm wavelengths. The detection results are shown in the figure 6.

The results show that the fluorescence intensity of the GOM-HCEr® group was significantly lower than that of the blank control group, indicating that the intake of ergothioneine can effectively inhibit skin glycation reactions. This suggests that it not only improves the surface skin condition but may also block the glycation chain at the molecular level, slowing down the aging of collagen in the dermis and delaying the aging process from its root cause.

5. Conclusions

This study shows that GOM-HCEr®, as a natural plant - derived active ingredient, combined with the theoretical basis of cell biology and modern clinical evidence, can significantly improve skin gloss, elasticity, water content, and anti - wrinkle ability after 28 days of oral intake, while reducing the level of glycosylation products, showing good anti - aging potential. This study provides an example for the integrated development of cytology and functional nutritional supplements, and also reflects the practical guiding significance of cell biology theory in the field of anti - aging. In the future, further research can be carried out from the perspective of modern medicine to explore the synergistic mechanism of *Pleurotus citrinopileatus* and other tonic herbs, so as to expand its application value in the field of skin care and anti - aging.

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