

UNIFINE® is material produced by fermenting soy extract containing isoflavones with *Aspergillus saitoi*.



Anti-aging and frailty prevention by anti-glycation actions

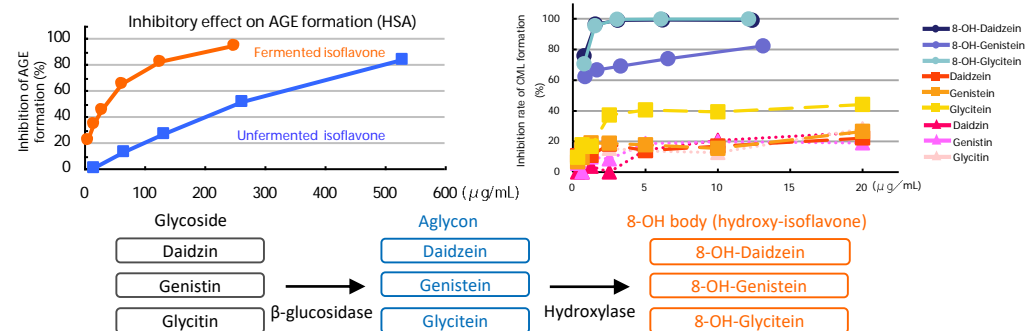
- Anti-glycation material containing hydroxylated isoflavones as its active ingredients. (Patent No. 5318339)
- Suppressing production and the decomposing of advanced glycation end products (AGEs)
- Our human-ingestion test showed the following :
 - Anti-glycation and antioxidant effects in the body
 - Skin rejuvenation and skin lightening effect
 - The effect to reduce glycation-induced degradation of bone quality
 - The effect to improve brain functions (effect of increasing neurotrophic factors and improving cognitive functions) Patent pending
 - Anti-inflammatory effect (Reduction of Inflammatory cytokine)
- Suppression of hair loss due to glycation damage, improvement of hair quality and hair growth.
- Anti-diabetic (improved glucose tolerance) and anti-obesity (suppressed fat accumulation) effects were confirmed.

Improvement of anti-glycation function by fermentation: Active ingredient of hydroxy-isoflavone

Anti-glycation: Inhibition of the glycation of human serum albumin/inhibition of CML formation. Regarding fermented isoflavone and unfermented isoflavone, the inhibitory effect on AGE formation was assessed via the glycation reactions of glucose and HSA (human serum albumin).

As a result, fermented isoflavone was confirmed to have an extremely high inhibitory effect on fluorescent AGE formation compared to unfermented isoflavone.

In addition, it was confirmed the inhibitory activity of isoflavones was also examined for CML production. Daidzein and genistein, which are aglycones, than daidzin and genistin, which are glycosides, and hydroxylated derivatives such as 8-OH-daidzein and 8-OH-genistein have much higher inhibition of CML formation. From these results, Hydroxy-isoflavone was confirmed to have strong anti-glycation activities compared to aglycon and glycoside.

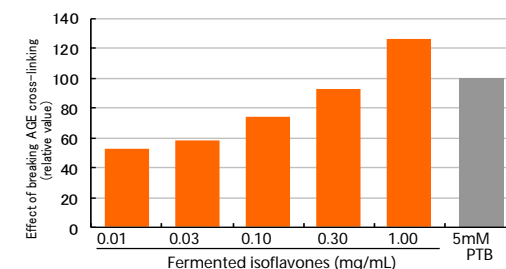
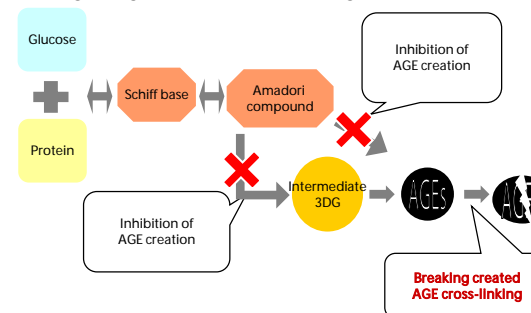


Product Name	UNIFINE®	
Name	Fermentation extract powder of soy bean extract	
Example of description of raw materials	Dextrin, Fermentation extract powder of soy bean extract	
Standard amount to be used	100 mg/day	
Package	1 kg/aluminum bag	
Storage	Store it away from direct sunlight and high temperature/humidity	
Expiration date	3 years from production date	
Specifications	Description	Test Method
Appearance	Pale yellow powder with characteristic odor	Visual
8-OH Isoflavone	More than 5%	HPLC Method
Isoflavone	Actual measured value	HPLC Method

Effect of breaking AGE cross-linking

Dicarbonyl compound exists as an intermediate during the creation of AGEs. Dicarbonyl compound is even more reactive than glucose and is an important component, as it largely contributes to the formation of AGEs. The level of dicarbonyl compound is high in the plasma of patients with diabetes, which is thought to largely contribute to the development of complications. It has also been revealed that a dicarbonyl structure is one of the cross-linking structures between proteins formed by the creation of AGEs. Therefore, the development of substances that disconnect a carbon-carbon bond in the dicarbonyl compound and that inhibit AGE accumulation and the cross-linking of proteins is considered not only useful for preventing and treating diabetes and complications, but is also important in aging prevention.

It has been confirmed that fermented isoflavones have the effect of breaking dicarbonyl compounds to inhibit AGEs from creating, along with an effect of breaking created AGEs.



*PTB (N-phenacyl thiazolium bromide): The effect of breaking cross-linking at an AGE-decomposing agent is validated.

The effect of improving brain functions through human ingestion of UNIFINE® (the effect of increasing neurotrophic factors)

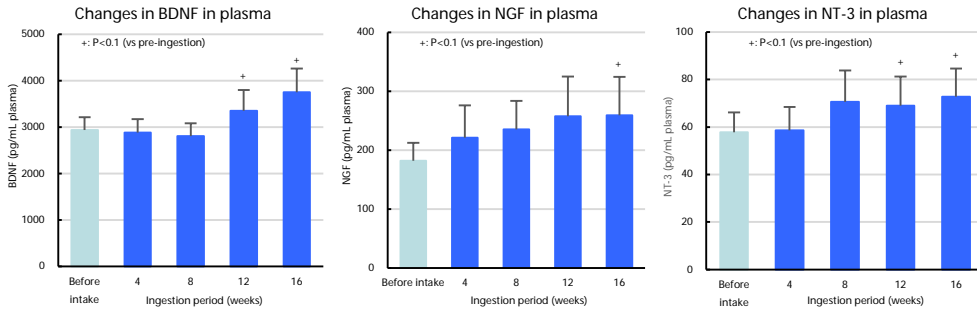
Neurotrophic factors are nutrients used for neuronal activities, therefore essential for the activities of the brain. Among them, Brain Derived Neurotrophic Factor (BDNF), Nerve Growth Factor (NGF), Nurotrophin-3 (NT-3) are widely distributed in the brain. The secretion of these neurotrophic factors decreases when we reach an elderly age, as well as brain functions.

Based on the above facts, the test was conducted to assess whether UNIFINE ingestion can improve brain functions by examining the impacts of UNIFINE ingestion on these neurotrophic factors.

<Test method>

- Subjects: 9 healthy adults (6 women, 3 men)
 - UNIFINE 100 mg/day (intake period of 16 weeks)
 - Test design: Comparison test between the before and after ingestion of test meals
- Blood samples were collected before ingestion, after 4, 8, 12, or 16 weeks of ingestion, and plasma was isolated. The concentration of each neurotrophic factor was measured.

BDNF, NGF, and NT-3 in plasma tended to rise over time as a result of the continuous intake of UNIFINE. The rates of increase in each neurotrophic factor from the values before ingestion to those of 16 weeks after ingestion were 27% for BDNF, 42% for NGF, and 25% for NT-3. Thus, the test showed that UNIFINE is expected to provide the effect of improving brain functions.



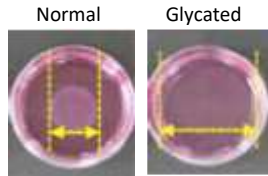
Effects of inhibiting collagen glycation for preventing sagging and improving resilience

<Test method>

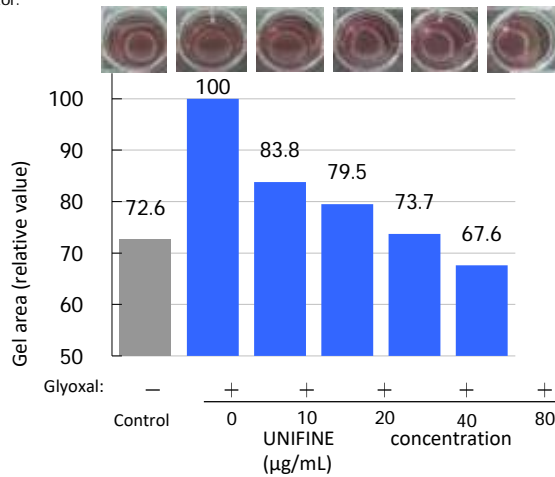
When fibroblasts are cultivated in type I collagen fibers, resilient collagen gel with a dermis-like structure is formed and contracts. However, this contractile activity is inhibited when the collagen is glycated, resulting in the collagen gel remaining spread out. In this test, the effect of inhibiting glycation for preventing sagging and improving resilience was confirmed by adding glyoxal (GO), a substance that promotes collagen glycation, and using collagen gel contractile activity as the indicator.

<Results>

When only GO is added, collagen glycation caused the collagen gel contractile activity to decrease. On the other hand, the addition of fermented isoflavone inhibited the decrease in contractile activity, resulting in the collagen gel remaining contracted. These results indicate that fermented isoflavone is effective for maintaining the contractile force of the collagen, thereby preventing skin sagging and improving skin resilience.



Normal: Resilient, and the collagen gel contracts.
Glycated: Less resilient, and the collagen gel remains spread out.



[Reference] Concentration converted from test data

*UNIFINE® can be converted from "fermented isoflavone" indicated in test data, as follows:
Conversion example: Fermented isoflavone: 1 µg = UNIFINE®: approx. 4 µg
Fermented isoflavone: 1 mg = UNIFINE®: approx. 4 mg
Fermented isoflavone: 1% = UNIFINE®: approx. 4%

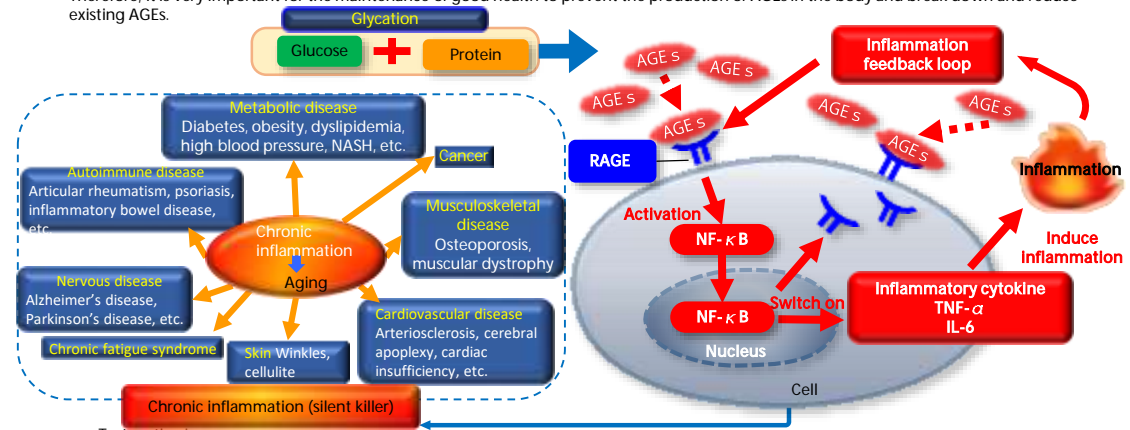
The effect of inhibiting inflammatory reaction caused by glycative stress (anti-inflammatory effect)

Mechanism of chronic inflammation through AGEs—RAGE bonding

RAGE (Receptor for Advanced Glycation Endproducts) is an AGEs receptor generated as the result of a glycation reaction. RAGE exists on the surface of many tissue cells, such as blood vessels, kidneys, lungs, the skin, and macrophages. When AGEs bonds with RAGE, a cell transcription factor protein (NF-κB) is activated, which then bonds with an inflammation causing gene and turns it on, triggering the production of an inflammation causing protein (Inflammatory cytokine: TNF-α, IL-6, etc.). At the same time, this promotes the synthesis of RAGE, resulting in an inflammation feedback loop that causes chronic inflammation and ultimately cell and tissue damage. In other words, glycative stress can be the cause of chronic inflammation (see the illustration below).

This chronic inflammation is said to be a **silent killer** and is attracting increased attention in the medical industry because it progresses without being noticed and could lead to an onset or progression of cancer, diabetes, arteriosclerosis, Alzheimer's disease, decreased immune function, and other diseases, as well as aging.

Therefore, it is very important for the maintenance of good health to prevent the production of AGEs in the body and break down and reduce existing AGEs.



<Test method>

- Test subjects: 9 healthy adults (6 female, 3 male)
- Ingest 100 mg of UNIFINE per day (for 16 weeks)
- Test design: Compare the before and after of ingesting UNIFINE

Take a blood sample before ingestion and at 16 weeks of ingestion. After isolating the blood plasma, measure the concentration of inflammatory cytokine (TNF-α and IL-6).

It was confirmed that continuous ingestion of UNIFINE lowers both TNF-α and IL-6 in blood plasma.

As stated above, because it was confirmed that continuous ingestion of UNIFINE significantly decreases AGEs in the blood and the skin over time. By inhibiting chronic inflammation which is the result from AGEs-RAGE bonding, UNIFINE can be expected to inhibit aging and the occurrence of age-related diseases.

In addition, in the testing of AGEs (CML)-induced NF-κB activation using ATDC5 (mouse pre-chondrogenic cell line), it was confirmed that the fermented soybean isoflavone and each isoflavone hydroxide inhibits NF-κB activation. Given this, isoflavone hydroxide generated through fermentation is believed to be one of the active ingredients for anti-inflammatory action.

