Product introduction

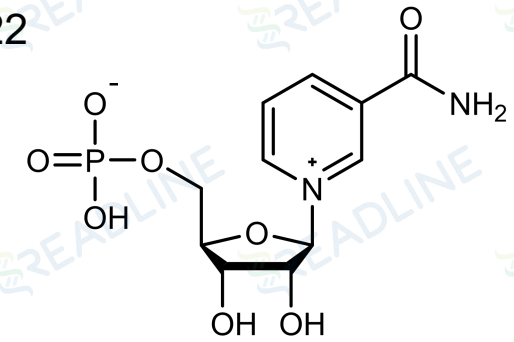
Readline® Healthcare

01

β-Nicotinamide Mononucleotide

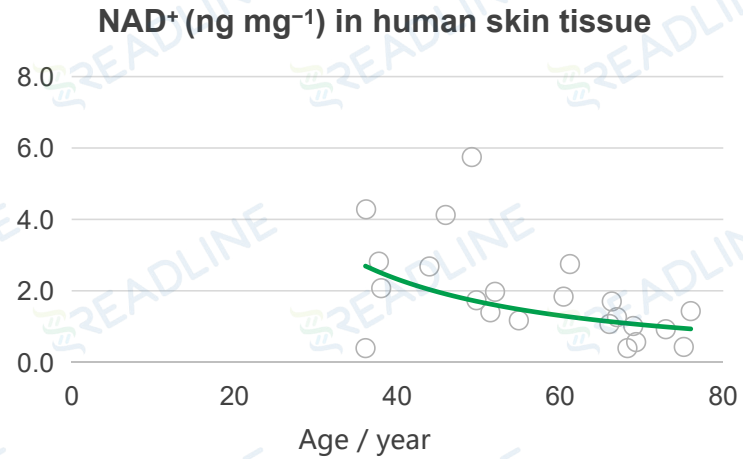
Product information

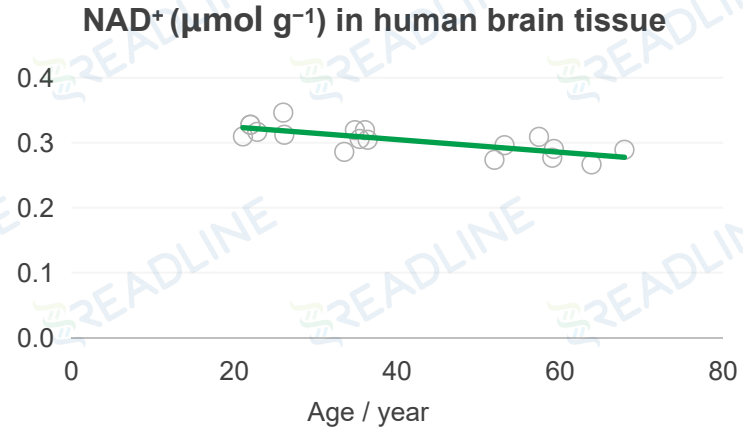
- **Product name:** β-Nicotinamide Mononucleotide
- **Common name:** NMN
- **Recommended dosage:** 250−500 mg /day
- **CAS No.:** 1094-61-7
- **Molecular formula:** $C_{11}H_{15}N_2O_8P$
- **Molecular weight:** 334.22

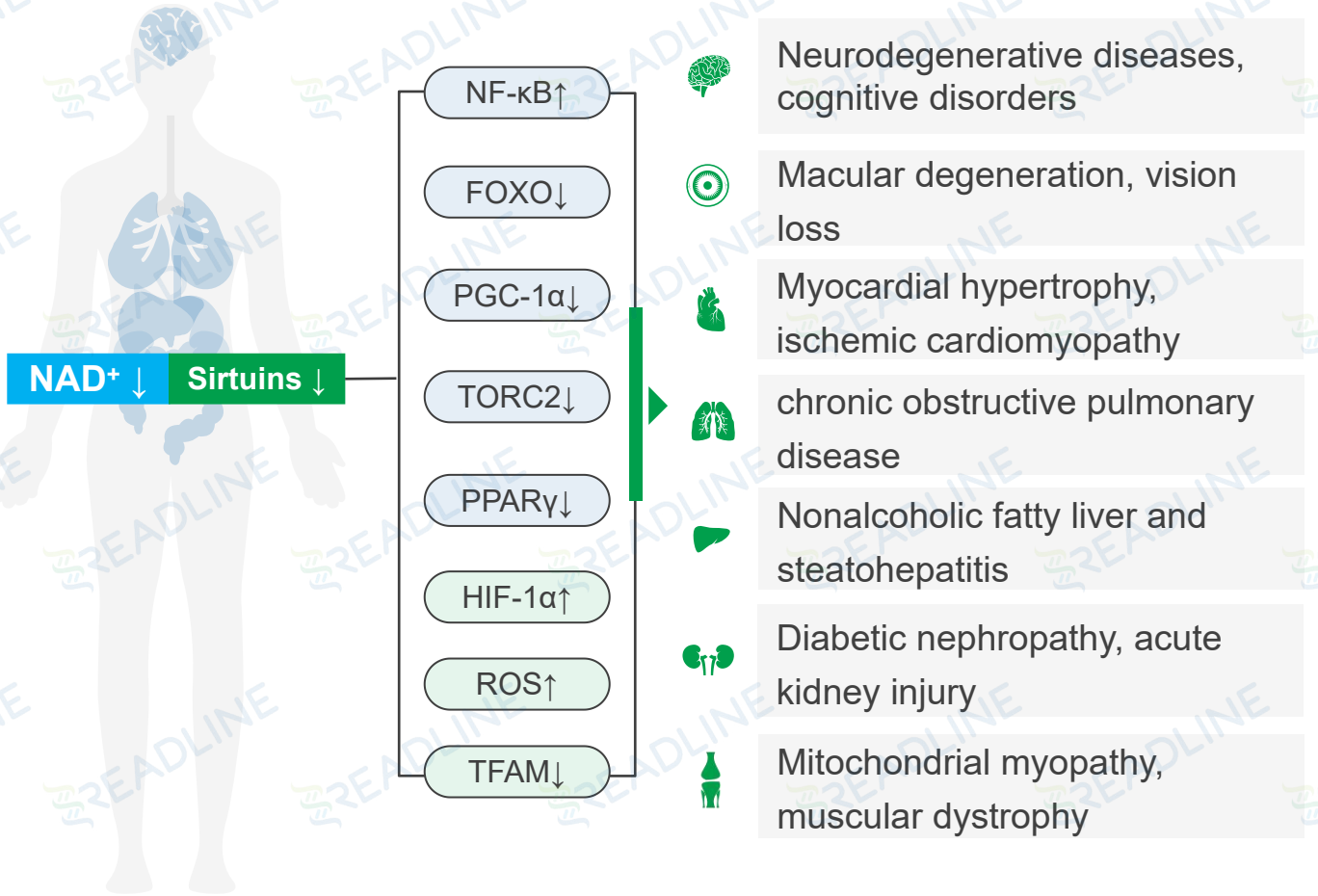


READLINE

Decreased NAD+ levels in the human body are associated with a variety of diseases

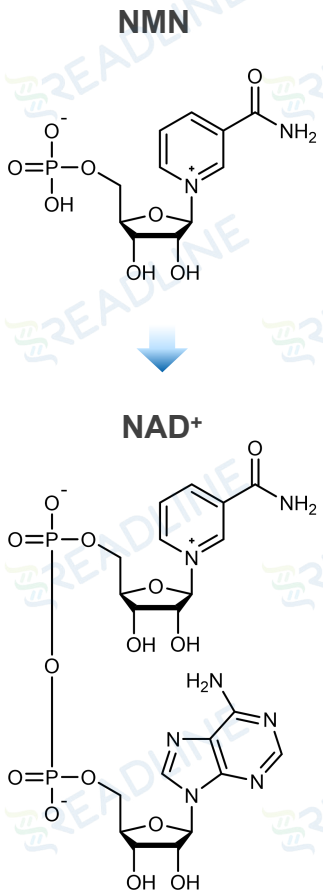




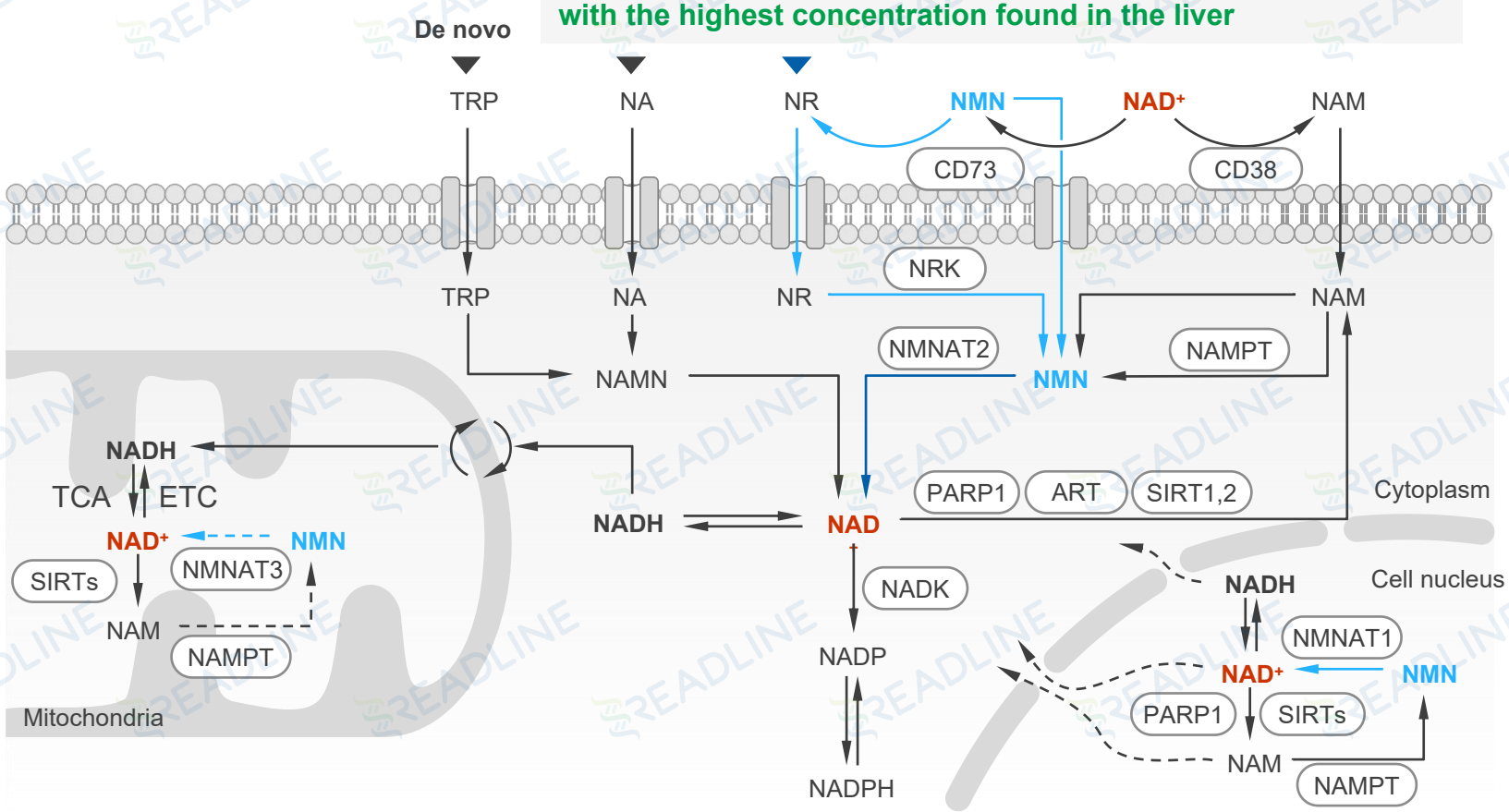


E. Verdin, *Science*, 2015, 350, 1208–1213; M. S. Bonkowski et al., *Nat. Rev. Mol. Cell Biol.*, 2016, 17, 679–690
L. Rajman et al., *Cell Metab.*, 2018, 27, 529–547; E. Katsyuba et al., *Nat. Metab.*, 2020, 2, 9–31
A. J. Covarrubias et al., *Nat. Rev. Mol. Cell Biol.*, 2021, 22, 119–141

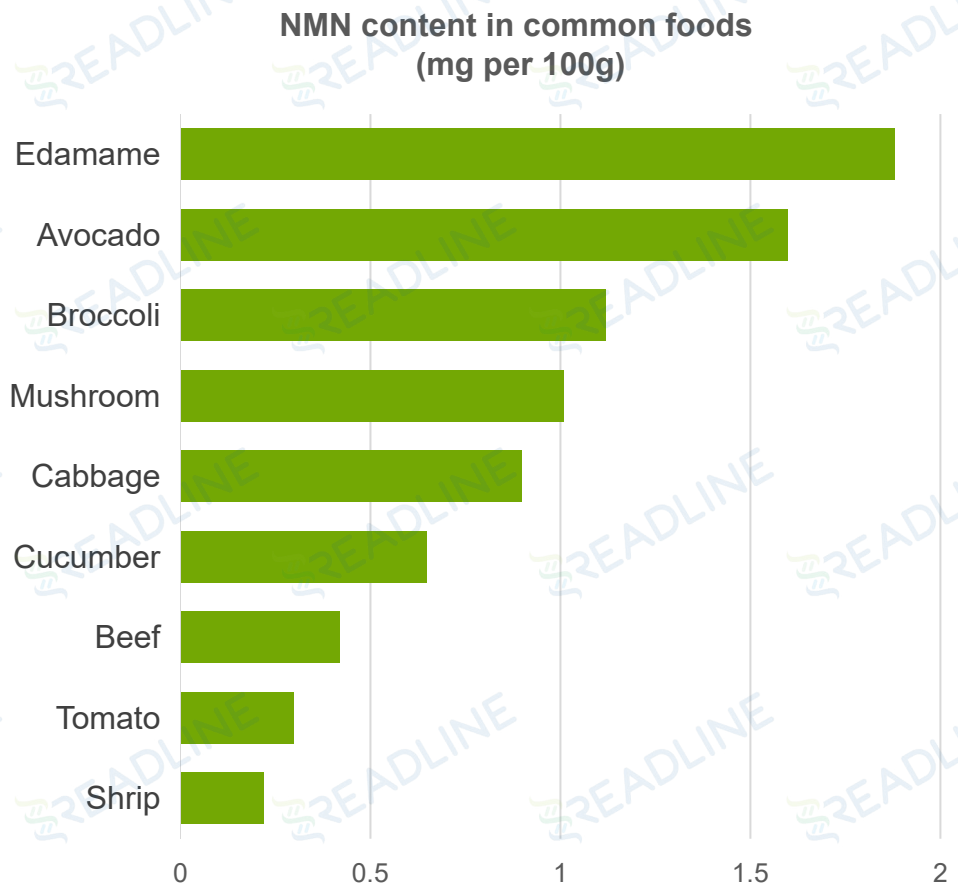
NMN is the best way to boost NAD+ levels



NRKs and NMNATs are expressed in various organ tissues, with the highest concentration found in the liver



The amount of NMN in natural foods is very limited



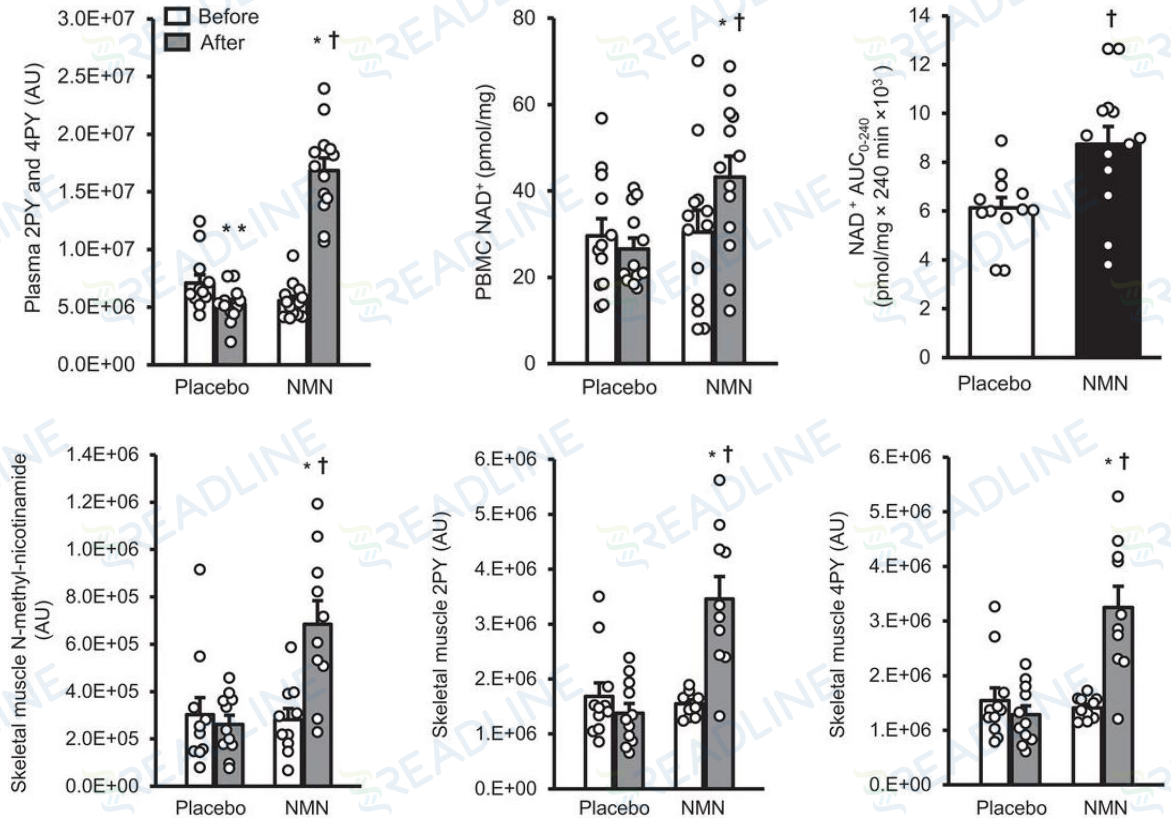
500 mg NMN ≈

25 kg

30 kg

It is difficult to obtain sufficient NMN solely from food intake!

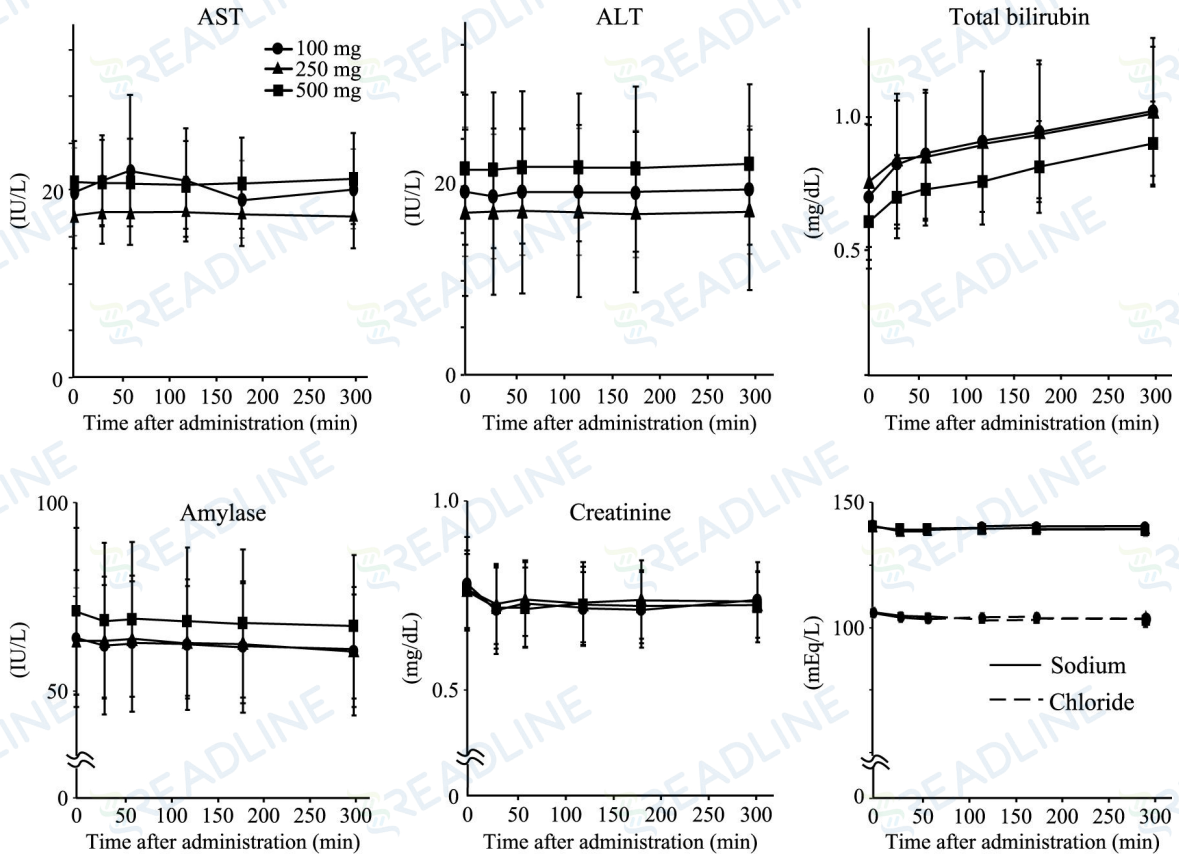
Effectiveness: NMN can increase the level of NAD+



- **Study Design:**
- A 10-week randomized, placebo-controlled, double-blind trial
- **Main results**
- After continuous oral administration of NMN for ten weeks (250 mg /day), the metabolites of NMN (2PY, 4PY) in plasma and muscle, as well as the NAD+ concentration in peripheral blood mononuclear cells (PBMC), were significantly higher compared to the control group.

M. Yoshino et al., *Science*, 2021, 372, 1224–1229

Safety: No adverse reactions after administration



- **Study Design:**
- Oral administration of NMN (100 mg, 250 mg, 500 mg)
- **Main results**
- After 5 hours, there were no significant fluctuations in clinical indicators such as blood pressure, heart rate, oxygen saturation, and serum biochemical markers in the subjects.

J. Irie et al., *Endocr. J.*, 2020, 67, 153–160

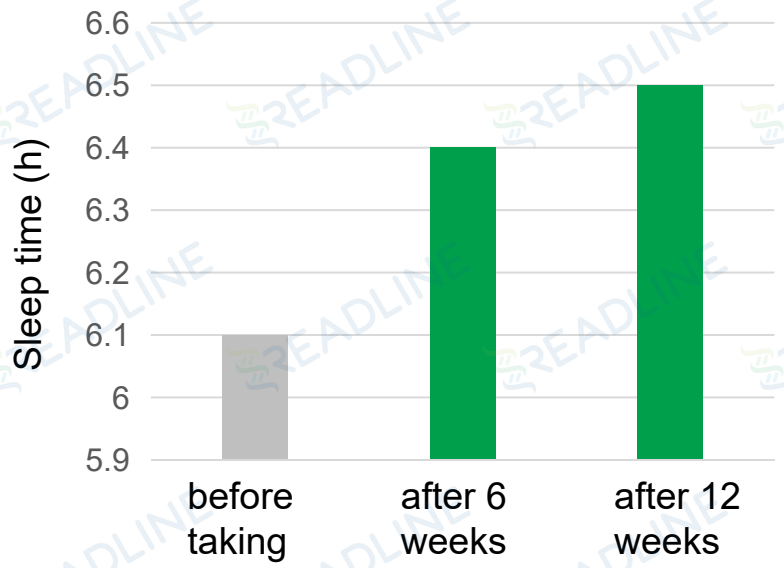
Mainstream Benefits of NMN

sleep immunity sports bones nervous system liver

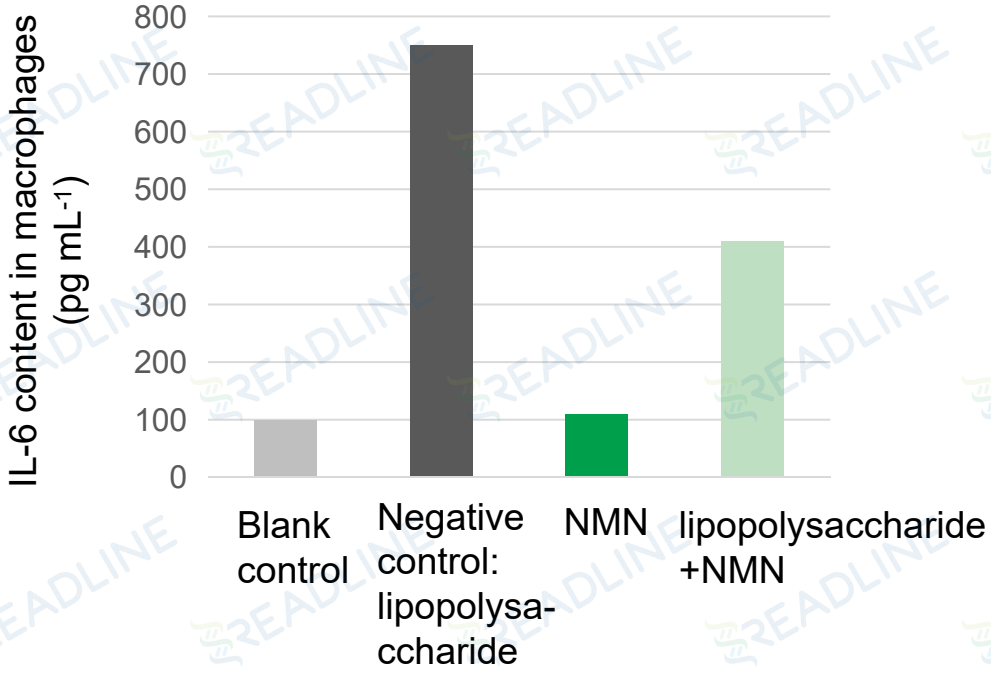
READLINE

Efficacy correlation experiment

- Sleep improvement



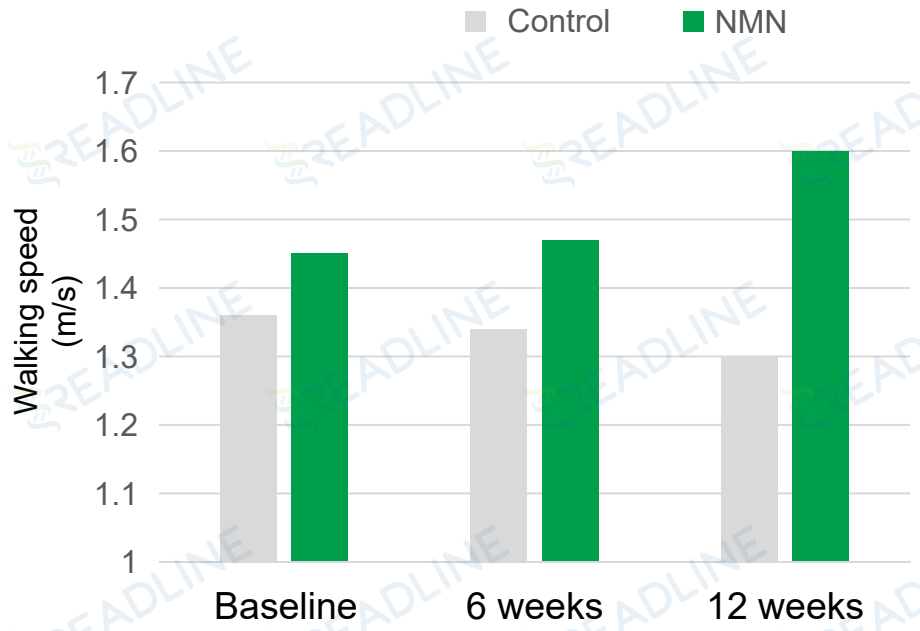
- Enhance immunity



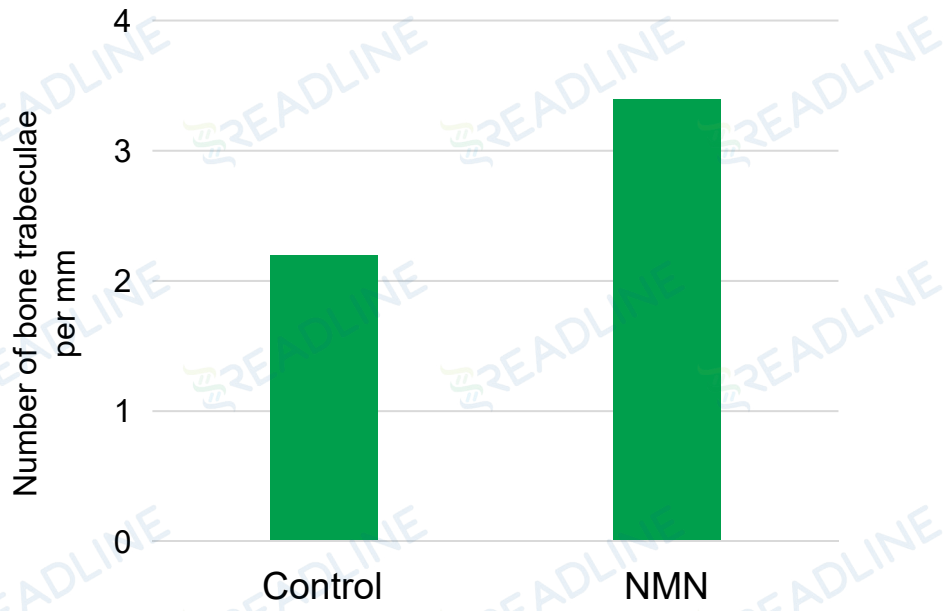
M.Kim et al., *Nutrients*, 2022, 14, 755-768
J.Liu et al., *Frontiers in Molecular Biosciences*, 2021, 7, 8, Article 702107

Efficacy correlation experiment

Boost athletic performance



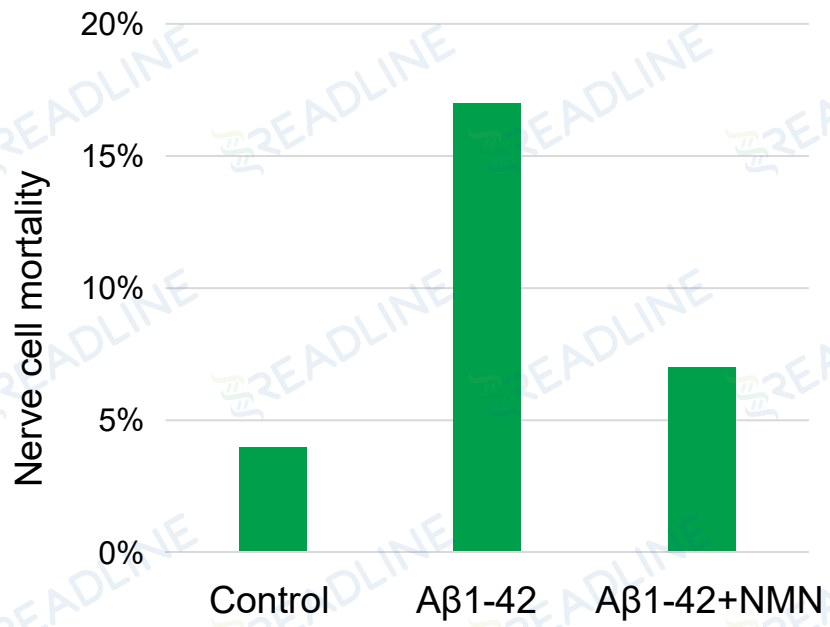
Strengthen bones



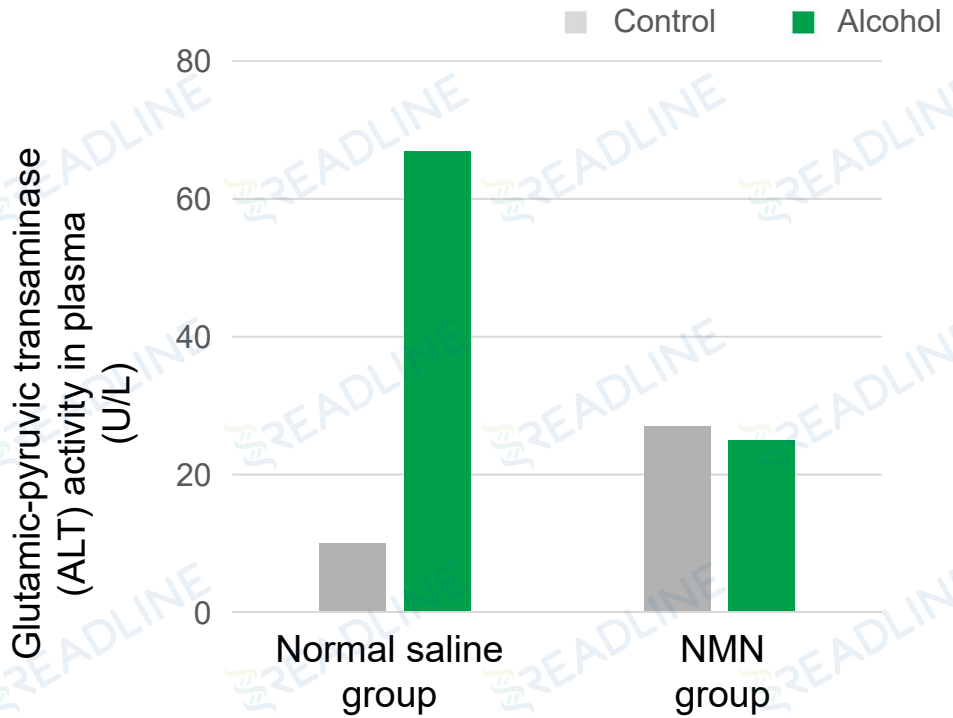
M.Igarashi et al., *Npj Aging Mech. Dis.*, 2022, 5, 8, 1-53
Song et al., *Cell Death Dis.*,2019, 10, 336-347

Efficacy correlation experiment

- Protect the central nervous system



- Protect liver



X.Wang et al., *Brain Res.*, 2016, 1643, 1-9
Assiri et al., *Human Genomics.*, 2019, 13: 65-77

Group standard setting participant

ICS 07.100.99
CCS X69

CASME

团　　体　　标　　准

T/CASME 011—2021

进出口用原料质量标准 β-烟酰胺
单核苷酸（生物法）

Quality standards for raw materials used for import and export
β-Nicotinamide Mononucleotide（Biological method）

2021-11-10 发布　　2021-11-20 实施

中国中小商业企业协会　发布

前　言

本文件按照GB/T 1.1—2020《标准化工作导则　第1部分：标准化文件的结构和起草规则》的规定起草。请注意本文件的某些内容有可能涉及专利，本文件的发布机构不应承担识别这些专利的责任。

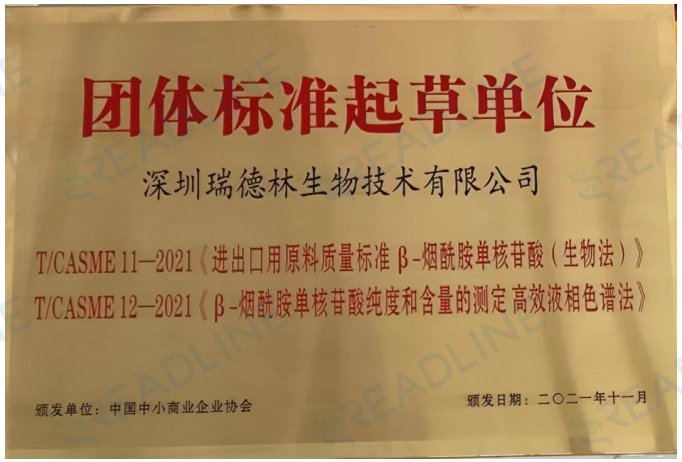
本文件由中国检验检疫科学研究院粤港澳大湾区研究院和基因港（香港）生物科技有限公司提出。

本文件由中国中小商业企业协会归口。

本文件起草单位：中国检验检疫科学研究院粤港澳大湾区研究院，基因港（香港）生物科技有限公司，深圳瑞德林生物技术有限公司，尚科生物医药（上海）有限公司，余姚莱孚斯本健康科技有限公司，苏州华赛生物工程技术有限公司，南通和康生物科技有限公司，音美医药科技（上海）有限公司，克洛怡制药有限公司，吉林百奥生物科技有限公司，DOLWORTH MARKETING PTELTD，重庆智源医创研究院有限公司，株式会社欧澤，中美原实业（上海）有限公司，深圳希吉亚生物技术有限公司，中国检验检疫科学研究院检测中心，LANTERN SKINCARE INSTUTUTE INC，上海途零信息科技有限公司，国正检验认证有限公司，中检科创（北京）测试认证有限责任公司，中检科（北京）测试技术有限公司，标管准家（北京）标准化服务中心。

本文件主要起草人：乐粉鹏，王骏，王桂林，刘建，竺伟，范相龙，李洋，胡志浩，李鹏飞，王勇，任再杰，姚立国，余建军，闫雪钰，NICK PHAN，赵荣之，李鹏程，曾淞焯，李钊，张志强，周立成，林博，王云帆，宋小莉，袁吉泽，孟妍，郭汉文，别致，赵亚洲，陈航宇，郑晓。

本文件为首次发布。



Complete production qualification

- FDA cGMP
- FSSC22000
- ISO9001
- ISO45001
- Halal, Self-GRAS

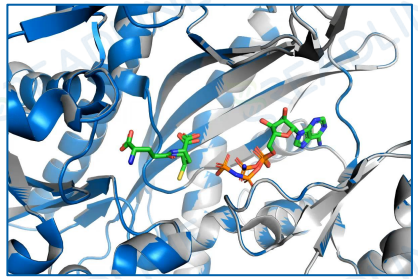
Technical advantage: cost leadership

China Patent
CN 112795606B

1 Design

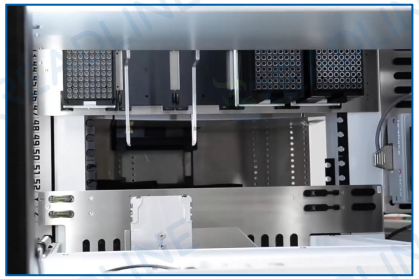
- Computer aided protein design
- Design of gene element screening scheme

2 Modification



- Conversion rate increased to 98%
- Catalytic activity increased by more than 1000 times

3 Screening



- Screening throughput increased by 50 times
- Shorten the R&D cycle by at least 60%

4 Industrialization

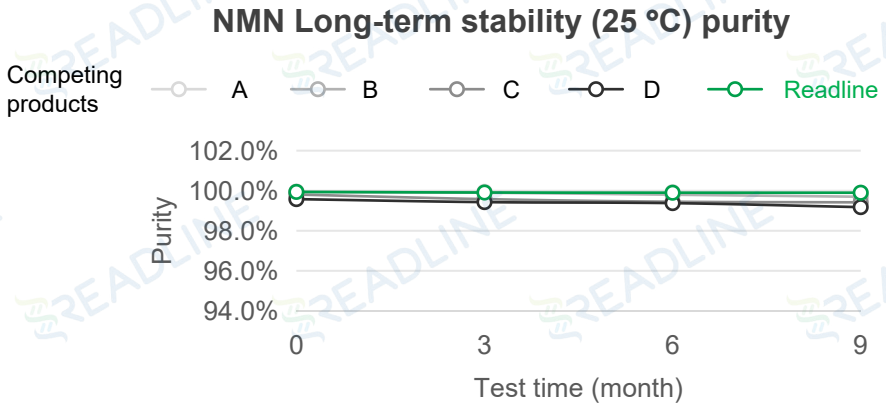
- Product cost reduction

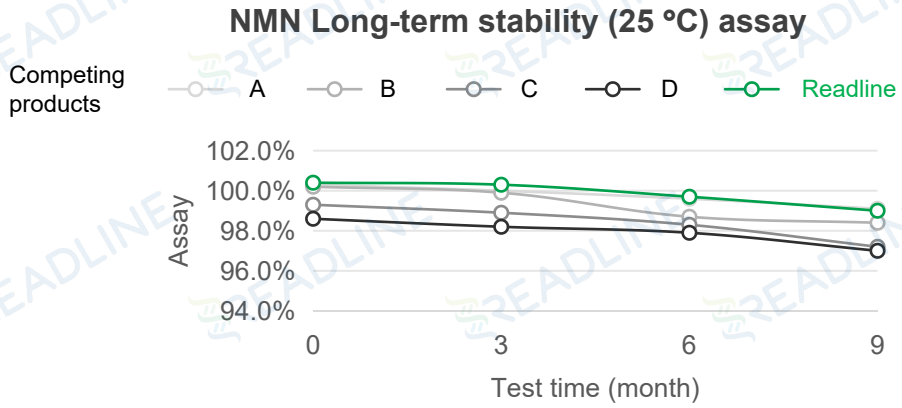
READLINE

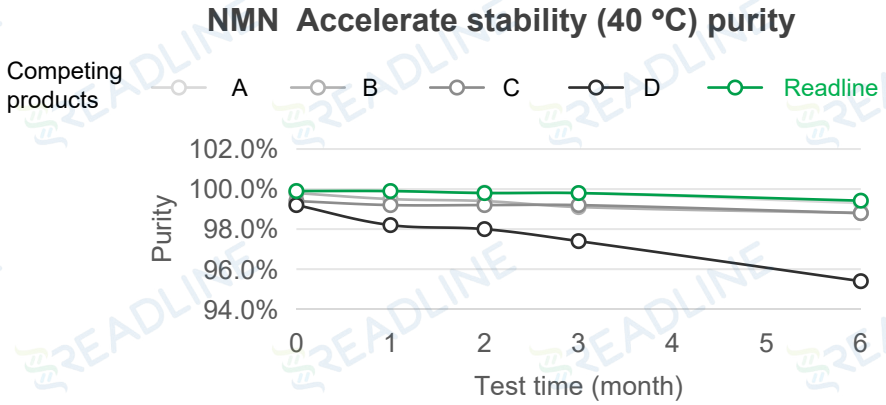
NMN Product Appearance

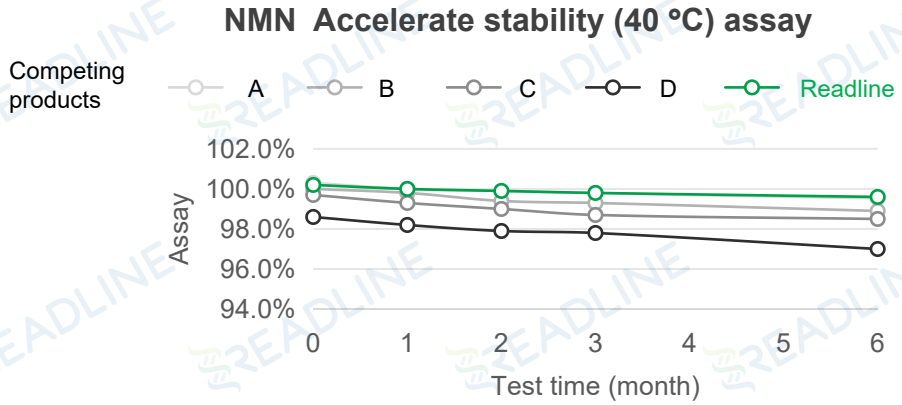
NMN Liquidity

Stability test of NMN









NMN stability test: product appearance

25 ℃ Long-term storage of NMN powder color change

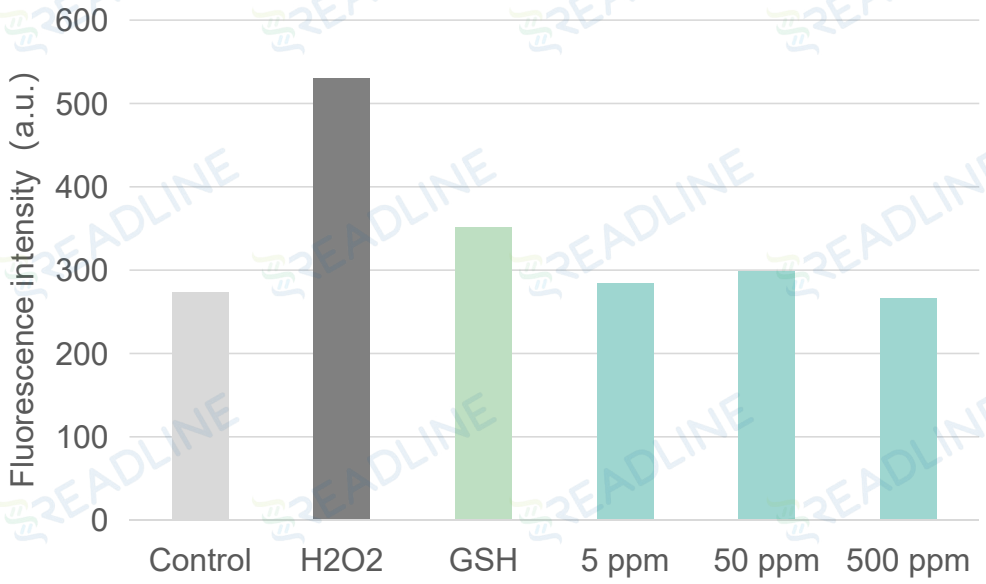
Test duration (month)	Readline	Prooduct A	Prooduct B	Prooduct C	Prooduct D
0	White-like crystalline	White-like crystalline	White-like crystalline	White powder	White powder
3	White-like crystalline	White-like crystalline	White-like powder	White powder	Yellowish powder
6	White-like crystalline	White-like crystalline	White-like powder	Yellowish powder	Yellowish powder
9	White-like crystalline	White-like crystalline	White-like powder	Yellowish powder	Yellowish powder

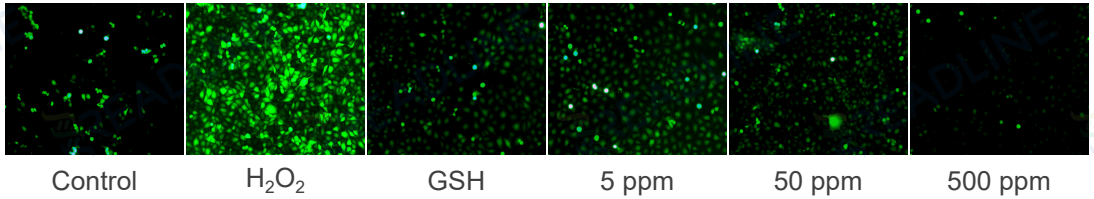
40 ℃ accelerated NMN powder color change

Test duration (month)	Readline	Prooduct A	Prooduct B	Prooduct C	Prooduct D
0	White-like crystalline	White-like crystalline	White-like crystalline	White-like powder	White-like powder
1	White-like powder	White-like powder	Yellow powder	Yellow powder	Yellow powder
3	Yellowish powder	Yellowish powder	Yellow powder	Yellow powder	Yellow powder
6	Yellowish powder	Yellowish powder	Yellow powder	Yellow powder	Yellow powder
9	Yellow powder	Yellow powder	Yellow powder	Yellow powder	Yellow powder

In vitro

Antioxidant: NMN can reduce ROS

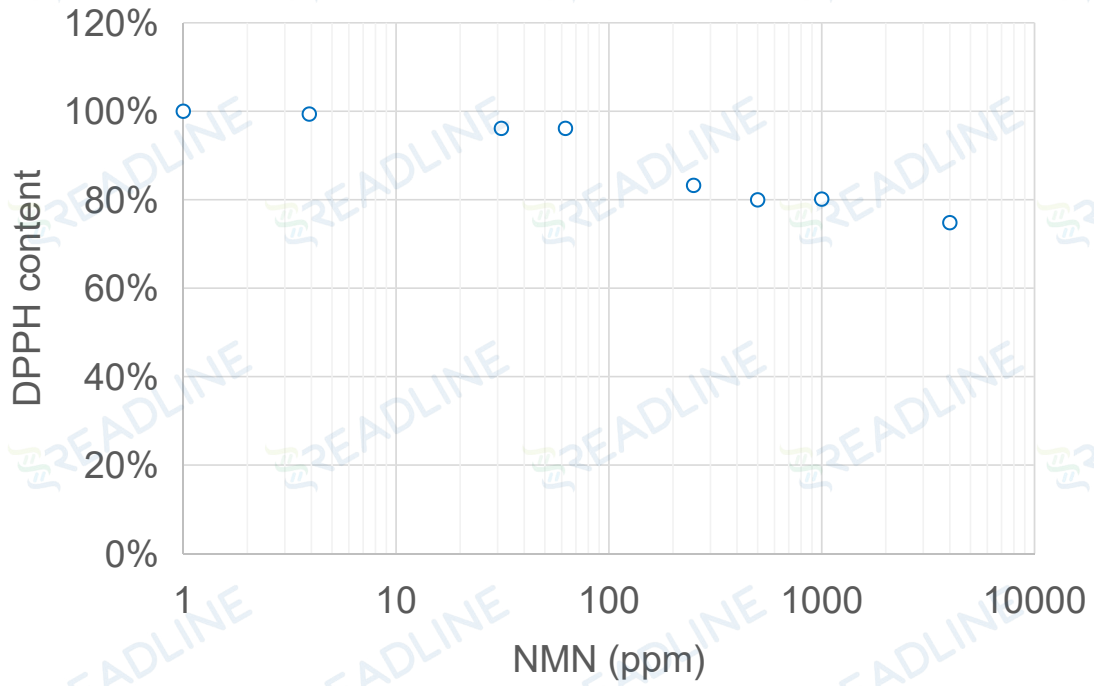




In vitro	HaCaT (P5)	24 h
Control	Medium	
Negative control	200 μM H_2O_2	
Positive control	100 ppm GSH	
Experimental group	NMN (5, 50, 500 ppm)	
Method	ROS fluorescence intensity	
Department of detection	Readline Efficacy Laboratory	

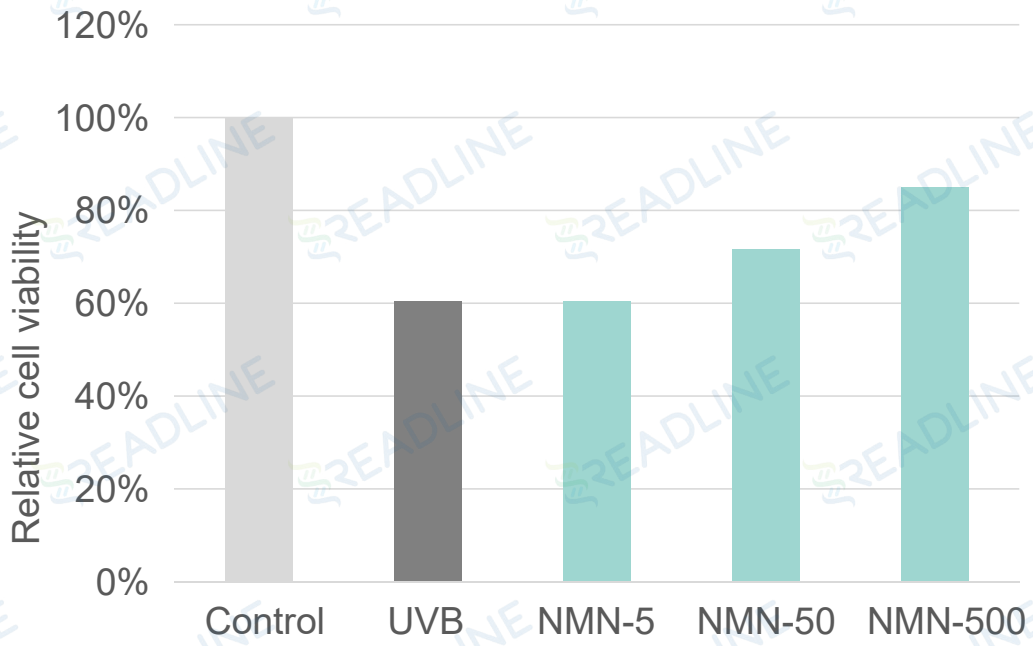
In vitro

Antioxidant: NMN can reduce DPPH (free radical)



Experimental group	NMN
Method	TECAN automated program
Department of detection	Readline Efficacy Laboratory

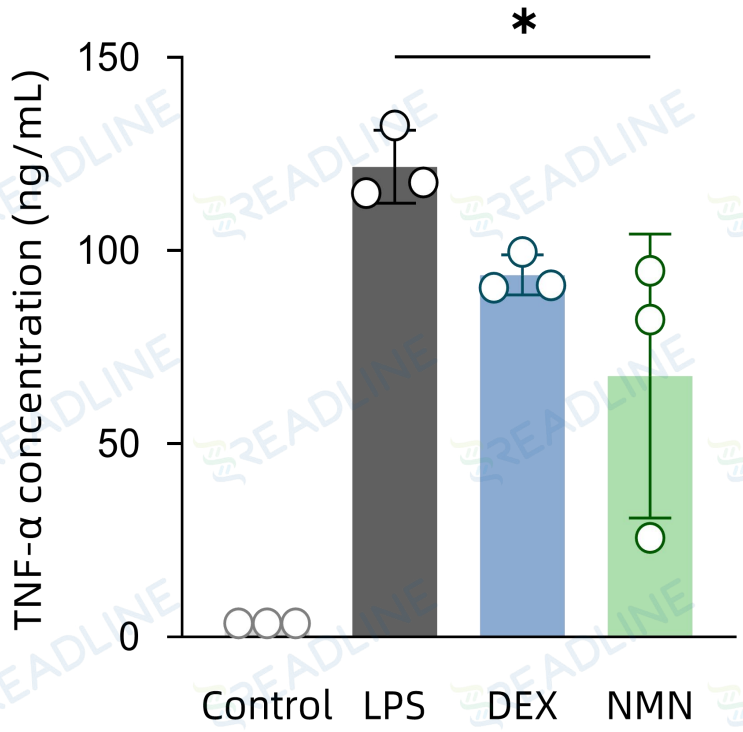
Repair: NMN can protect cells from UV damage



In vitro	HaCaT
Control	Medium
Negative control	UVB
Experimental group	NMN (5, 50, 500 ppm)
Method	ROS fluorescence intensity
Department of detection	Readline Efficacy Laboratory

In vitro

Anti-inflammatory: NMN can inhibit the expression of TNF-α



In vitro	RAW264.7 (P4)
Control	Medium
Negative control	1 ppm LPS
Positive control	100 ppm DEX
Experimental group	100 ppm NMN
Method	Detect the expression of TNF-α
Department of detection	Readline Efficacy Laboratory

Market application

Product Picture					
Brand	新兴和	Herbalmax	ESMONG	基因港	Fooubody
Origin	Japan	US	US	HongKong	US
Price	$3000	$400	$400	$200	$100
Specifications	60	60	70	60	60
Dosage / day	1-2	2	2	2	2
NMN Content /capsule	150mg	160mg	150mg	150mg	150mg

Market application

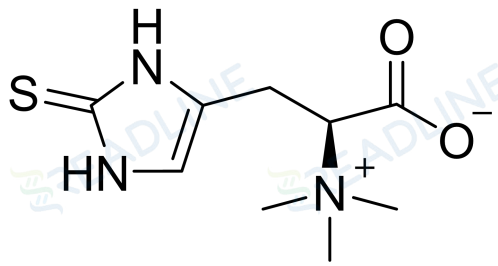
- Main form and dosage: Capusles, tablets, 125-500 mg
- The main origin of finish products: US, Japan
- Efficacy claim: NAD+ Booster
- Common combinations: Coenzyme Q10, PQQ, Vitamins, antioxidants

02

Ergothioneine

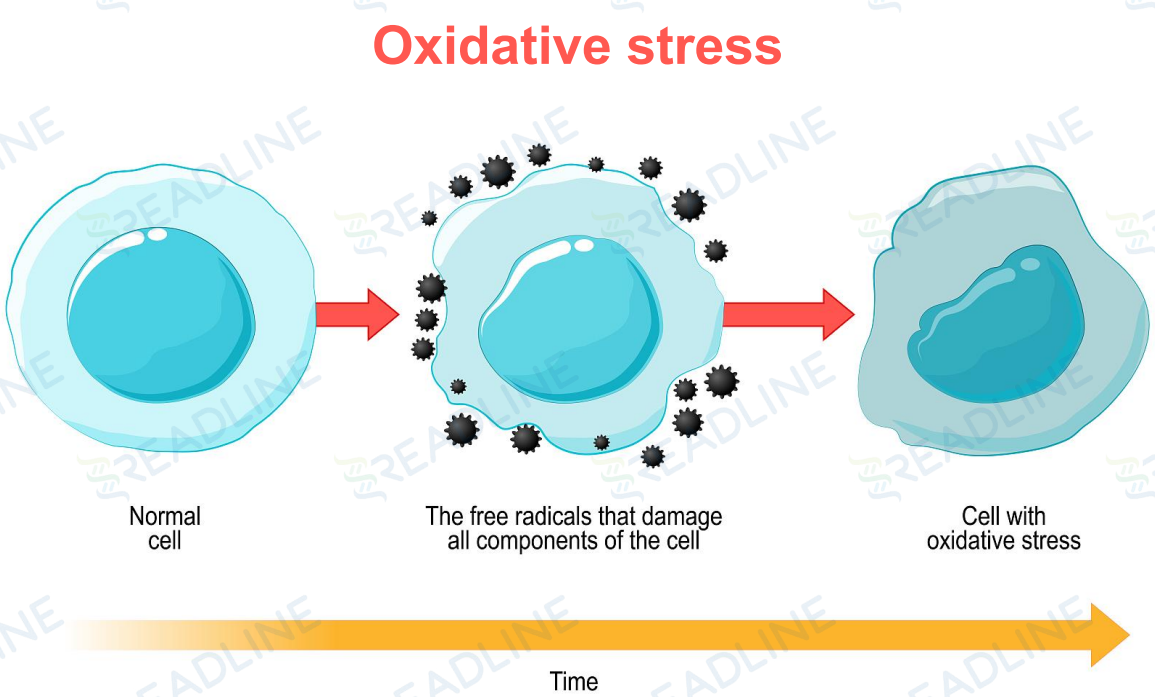
Product information

- **Chinese name：** 麦角硫因
- **Name：** Ergothioneine
- **CAS No.：** 497-30-3
- **EINECS No.：** 207-843-5
- **Molecular formula：** $C_9H_{15}N_3O_2S$
- **Molecular weight：** 229.3

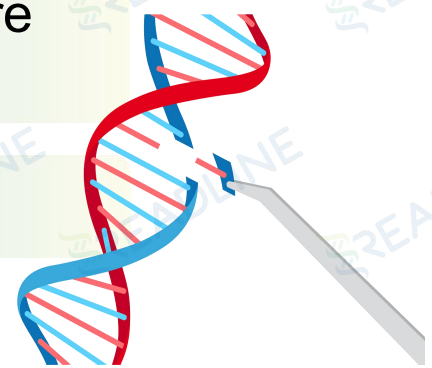


READLINE

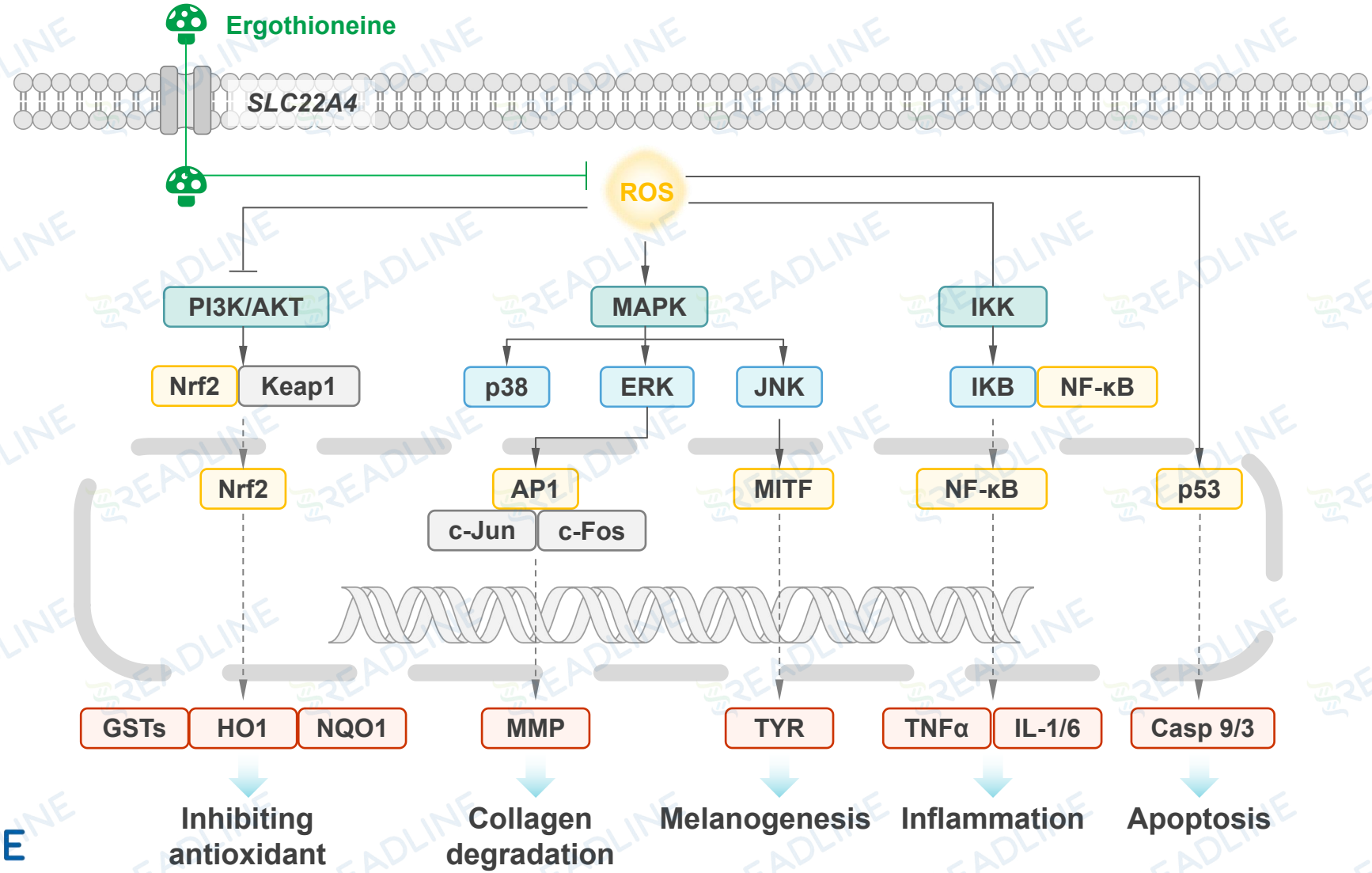
Reactive oxygen species cause oxidative stress in cells, leading to aging



- DNA damage
- Lipid damage, Cell membrane structure breakdown
- Mitochondrial damage
- Apoptosis
- Inflammatory response



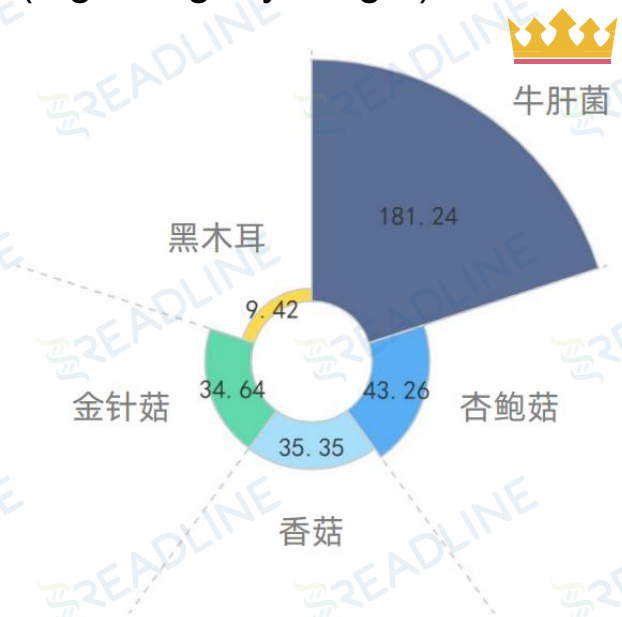
Molecular mechanism of ergothioneine



Sources of ergothioneine and its content in common foods

- Only certain bacteria and fungi can synthesize it
- Mammals, plants, humans can not synthesize on their own

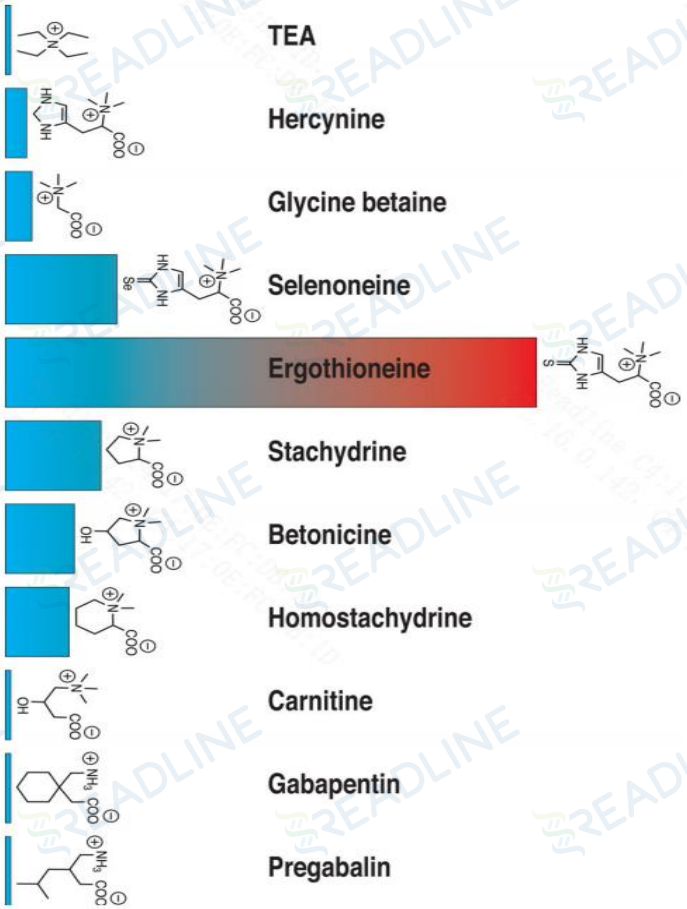
- Among common foods, the content of ergothione in edible fungi is higher (mg/100 g dry weight)

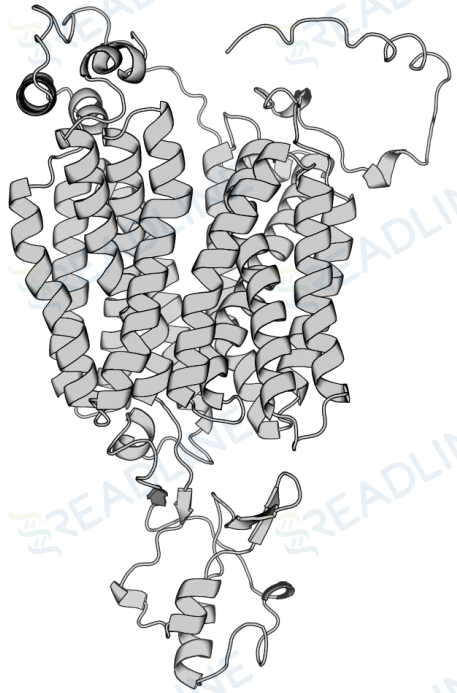


- Less in other kinds of foods (mg/1 kg dry weight)

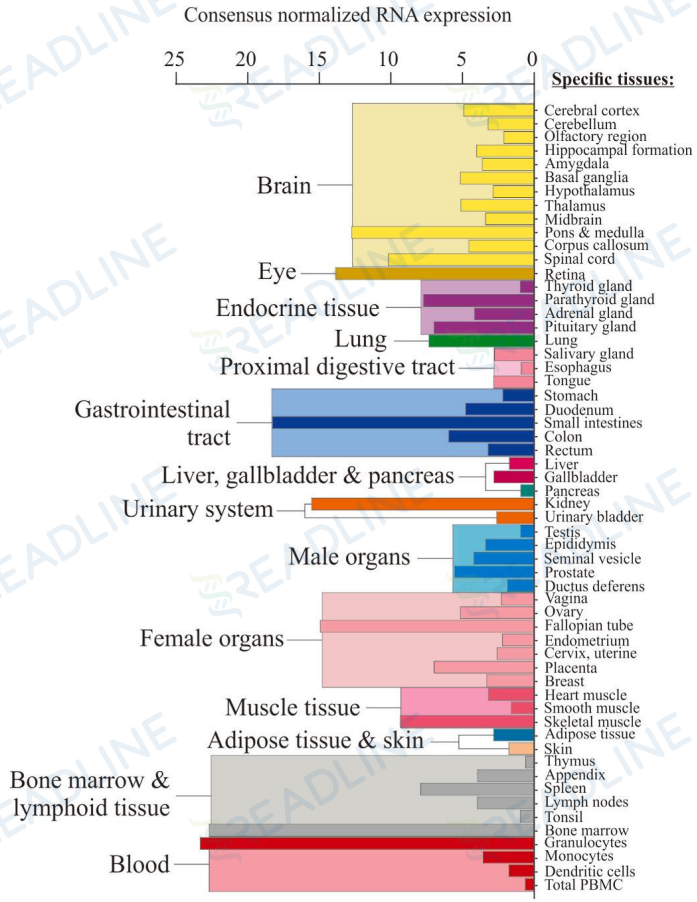
Halliwell, et al., *FEBS letters*, 2018, 592.20, 3357-3366.

The importance of ergothioneine: specific transport systems in the human body





Ergothionein transporter
ETT / OCTN1

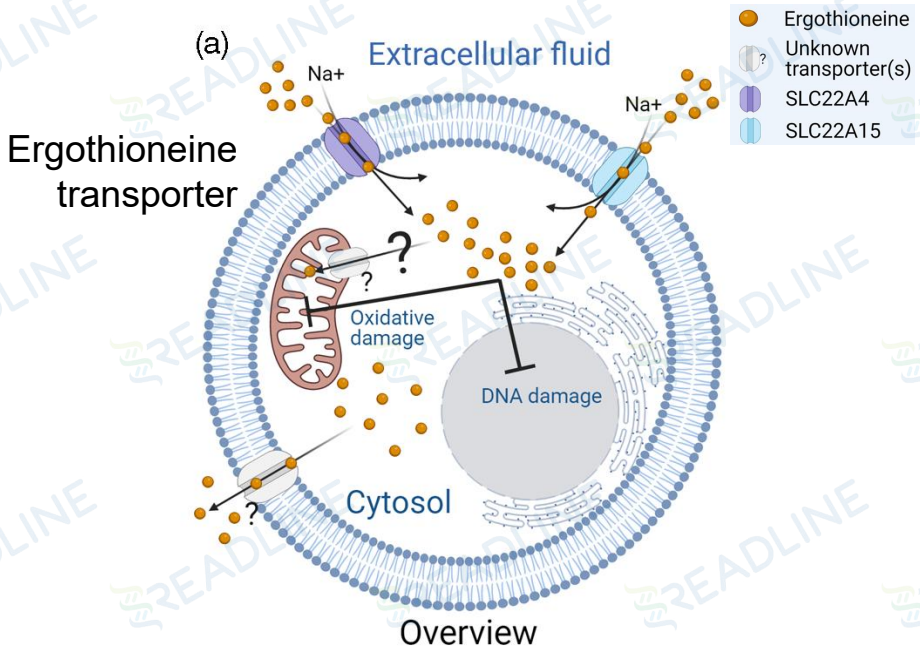


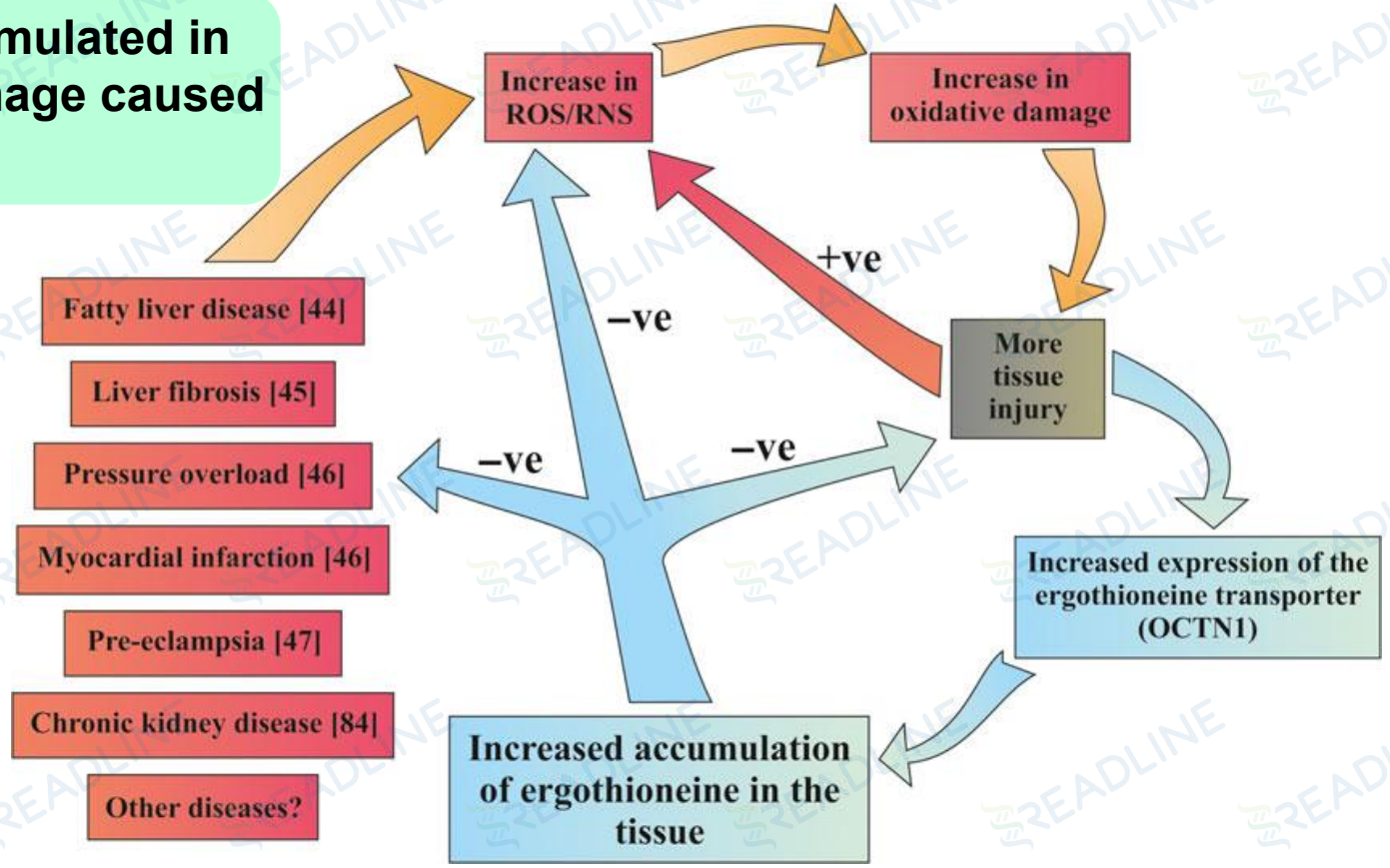
ETT is expressed in many tissues of human body

D. Gründemann et al., *FEBS Lett.*, 2022, 596, 10, 1252-1269
T.A. Kumosani, *Exp. Mol. Med.*, 2001, 31, 33, 1, 20-2

Ergothioneine is an adaptive antioxidant

Ergothione can be actively accumulated in damaged sites to repair cell damage caused by reactive oxygen species





B. Halliwell et al. *Biochem. Biophys. Res. Commun.*, 2016, 470, 245–250; B. Halliwell et al., *FEBS Lett.*, 2018, 592, 3357–3366

Recommended usage

SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 26 October 2016

doi: 10.2903/j.efsa.2016.4629

Safety of synthetic L-ergothioneine (Ergoneine®) as a novel food pursuant to Regulation (EC) No 258/97

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), Dominique Turck, Jean-Louis Bresson, Barbara Burlingame, Tara Dean, Susan Fairweather-Tait, Marina Heinonen, Karen Ildico Hirsch-Ernst, Inge Mangelsdorf, Harry J McArdle, Androniki Naska, Monika Neuhäuser-Berthold, Grażyna Nowicka, Kristina Pentieva, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Martin Stern, Daniel Tomé, Marco Vinceti, Peter Willatts, Karl-Heinz Engel, Rosangela Marchelli, Annette Pöting, Morten Poulsen, Josef Schlatter, Reinhard Ackerl and Henk van Loveren

Abstract

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver a scientific opinion on synthetic L-ergothioneine, marketed as Ergoneine®, as a novel food submitted pursuant to Regulation (EC) No 258/97 of the European Parliament and of the Council. The novel food, synthetic L-ergothioneine, is produced by a one-pot patented manufacturing process. Chemically, L-ergothioneine is a derivative of thiolhistidine, and it is naturally present in a number of foodstuffs such as mushrooms, some varieties of black and red beans, offal and cereals. The production process for the novel food is sufficiently described and does not raise concerns about the safety of the novel food. The information on the composition, specifications, batch-to-batch variability and stability of the novel food is sufficient and does not raise safety concerns. The applicant intends to use the novel food in quantities of up to 5 mg per serving in alcohol-free beverages, cereal bars, milk, fresh dairy products and chocolate. The applicant also proposes to provide the novel food as a food supplement, with a daily dose of up to 30 mg/day for adults and 20 mg/day for children. The target population is children above 3 years of age and the general adult population, except pregnant and breastfeeding women. Considering the NOAEL of 800 mg/kg bw per day, which was based on two subchronic toxicity studies in rats, and the maximum estimated intake levels for L-ergothioneine from all sources, the Panel concludes that the margins of safety of 470 for adults (except pregnant and breastfeeding women) and of 216 for children above 3 years of age are sufficient. The Panel concludes that the novel food, synthetic L-ergothioneine (marketed as Ergoneine®), is safe under the intended conditions of use as specified by the applicant.

Keywords: L-ergothioneine, Ergoneine®, novel food, ingredient, safety

Requestor: European Commission following an application by Tetrahedron

Question number: EFSA-Q-2015-00613

Correspondence: nda@efsa.europa.eu

SCIENTIFIC OPINION

EFSA Journal

ADOPTED: 25 October 2017

doi: 10.2903/j.efsa.2017.5060

Statement on the safety of synthetic L-ergothioneine as a novel food – supplementary dietary exposure and safety assessment for infants and young children, pregnant and breastfeeding women

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA), Dominique Turck, Jean-Louis Bresson, Barbara Burlingame, Tara Dean, Susan Fairweather-Tait, Marina Heinonen, Karen Ildico Hirsch-Ernst, Inge Mangelsdorf, Harry J McArdle, Androniki Naska, Monika Neuhäuser-Berthold, Grażyna Nowicka, Kristina Pentieva, Yolanda Sanz, Alfonso Siani, Anders Sjödin, Martin Stern, Daniel Tomé, Marco Vinceti, Peter Willatts, Karl-Heinz Engel, Rosangela Marchelli, Annette Pöting, Morten Poulsen, Josef Rudolf Schlatter, Reinhard Ackerl and Henk van Loveren

Abstract

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to provide a supplementary dietary exposure and safety assessment of synthetic L-ergothioneine for those groups of the population which had been excluded by the applicant in the original application, i.e. infants and young children (i.e. toddlers), pregnant and breastfeeding women. Thus, intake estimates were calculated for these population groups and the following maximum anticipated daily intakes of L-ergothioneine from the NF, in addition to the background diet, were calculated: 2.82 mg/kg body weight (bw) per day for infants, 3.39 mg/kg bw per day for toddlers and 1.31 mg/kg bw per day for adults including pregnant and breastfeeding women. The Panel considers that based on the overall toxicological data the no-observed-adverse-effect level (NOAEL) of 800 mg/kg bw per day as established in the original assessment also pertains to pregnant and breastfeeding women as well as to young children (i.e. toddlers) and infants. The corresponding margins of exposure (i.e. the ratio between the NOAEL and the maximum anticipated daily intakes) are 284 for infants, 236 for young children and 610 for pregnant and breastfeeding women. These margins of exposure are considered sufficient. The Panel concludes that the novel food, synthetic L-ergothioneine, is safe under the proposed uses and use levels for infants, young children (i.e. toddlers) and pregnant and breastfeeding women.

Keywords: L-ergothioneine, novel foods, food supplements

Requestor: European Commission

Question numbers: EFSA-Q-2017-00448

Correspondence: nda@efsa.europa.eu

GRAS Notice (GRN) No. 734
https://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/NoticeInventory/default.htm

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September 25, 2017

RECEIVED
SEP 28 2017
OFFICE OF
FOOD ADDITIVE SAFETY

Food and Drug Administration
Center for Food Safety & Applied Nutrition
Office of Food Additive Safety (HFS-255)
5001 Campus Drive
College Park, MD 20740-3835
Attention: Dr. Paulette Gaynor
Re: GRAS Notification—Ergothioneine

Dear Dr. Gaynor:

GRAS Associates, LLC, acting as the agent for Blue California is submitting for FDA review Form 3667 and the enclosed CD, free of viruses, containing a GRAS notification for *Ergothioneine*. Along with Blue California's determination of safety, an Expert Panel of qualified persons was assembled to assess the composite safety information of the subject substance with the intended use as an ingredient in select conventional foods and beverages at a maximum use level of 5 mg ergothioneine per serving. The attached documentation contains the specific information that addresses the safe human food uses for the subject notified substance as discussed in the GRAS guidance document.

If additional information or clarification is needed as you and your colleagues proceed with the review, please feel free to contact me via telephone or email.

We look forward to your feedback.

Sincerely,

(b) (6)

Katrina V. Emmel, Ph.D.
Senior Scientist/Associate
GRAS Associates, LLC
27499 Riverview Center Blvd., Suite 212
Bonita Springs, FL 34134
951-496-4178
emmel@gras-associates.com

Enclosure: GRAS Notification for Blue California - *Ergothioneine*

000001

A recommended daily dose of up to 30 mg/day for adults and 20 mg/day for children

EFSA J., 2016,14, 4629; *EFSA J.*, 2017, 15, 5060;

Difficult to Obtain Sufficient Ergothioneine Solely from Food

50-70 g
牛肝菌（湿重）

0.7 kg
灵芝

260-345 g
金针菇（湿重）

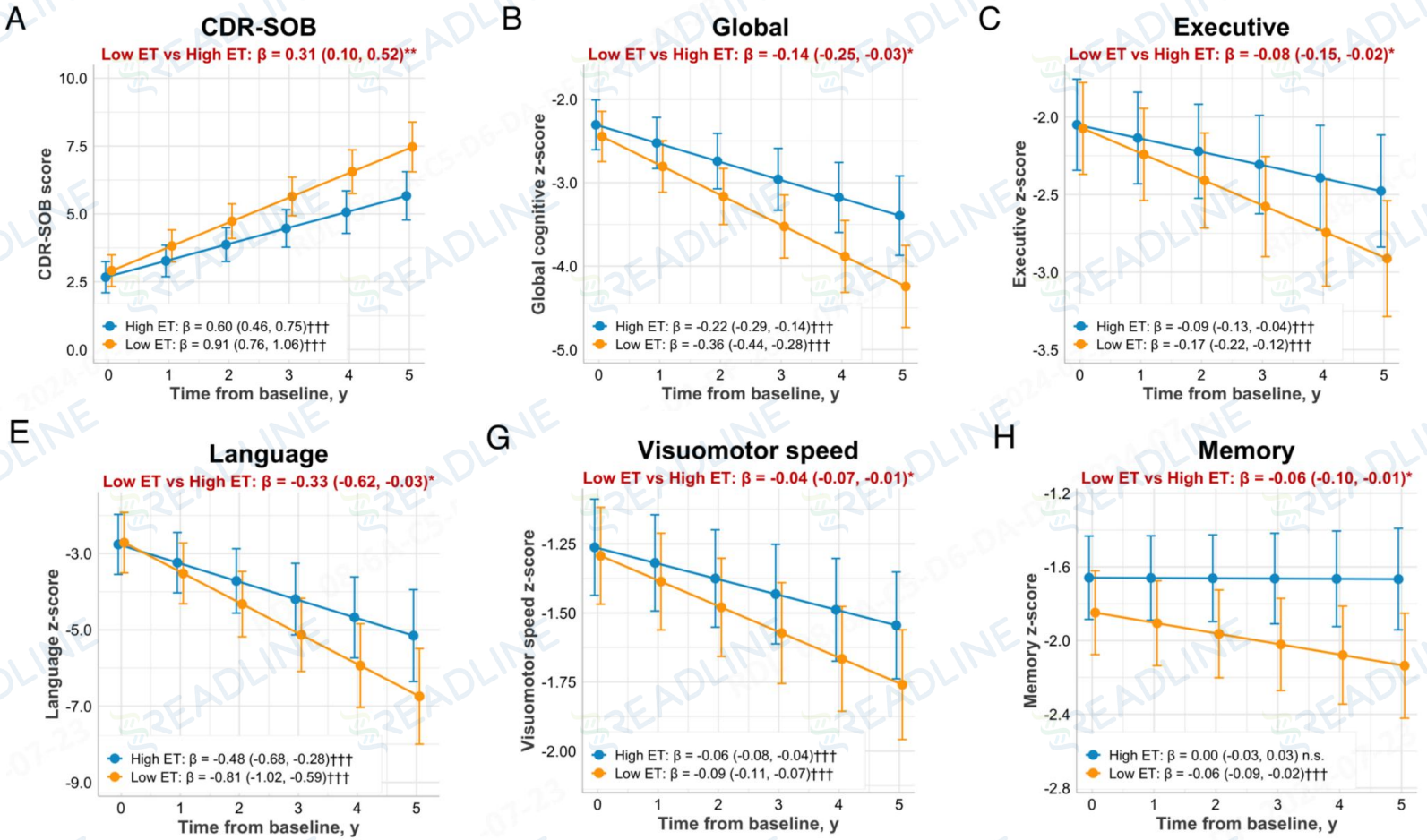
30 mg
Ergothioneine

7 kg
大蒜

260-345 g
香菇（湿重）

16 kg
燕麦

Ergothioneine is a biomarker for predicting cognitive decline in the elderly



High ET
Low ET

- CDR-SOB：clinical dementia score
- Global：overall cognitive level
- Executive：advanced cognitive functions

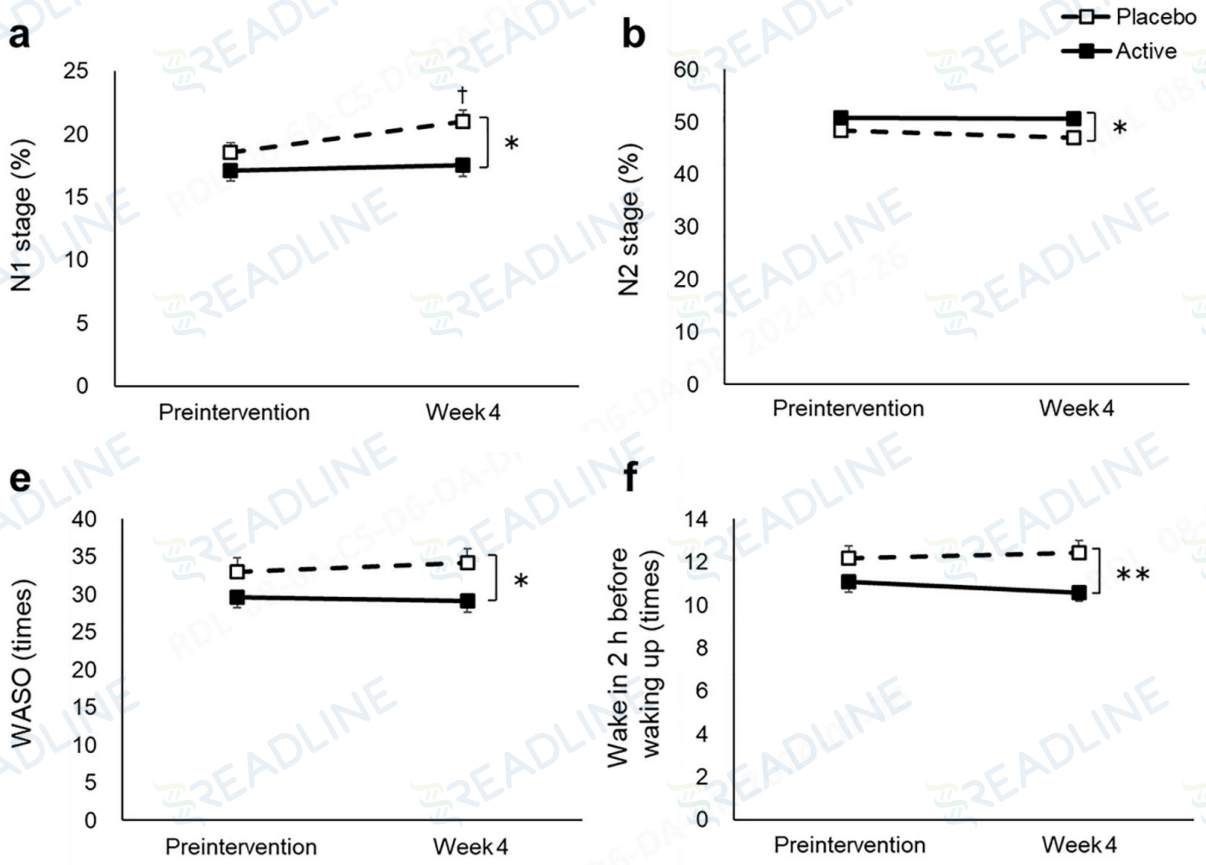
Conclusion

Plasma ergothioneine level can predict the development of multiple cognitive functions over 5 years

Wu L Y et al., *Antioxidants*, 2022, 11, 9, 1717

Ergothioneine can relieve difficulty falling asleep

- EEG measurements showed that EGT intake increased the N2 phase of non-rapid eye movement sleep and decreased the N1 phase, wakefulness, and frequency of awakening after sleep onset.



Makoto Katsube et al., *J. Funct.*, 2022, 95, 105165

Ergothioneine can improve cognition and sleep

Blue California完成ErgoActive®麦角硫因干预认知功能、记忆力和睡眠的开创性人体临床试验

Blue California completes groundbreaking human clinical trial on ErgoActive® ergothioneine intervention for cognitive function, memory, and sleep

GlobeNewswire | 2024-02-05 17:00 | 翻译由动脉网AI生成，点击反馈

P25-043-24 The Effect of Ergothioneine Supplementation on Cognitive Function and Other Health-Related Outcomes in Older Adults With Subjective Memory Complaints

Ian Zajac [1], Naomi Kakoschke [1], Linda May-Zhang [2]

[1] *CSIRO, Australia*

[2] *Blue California, Australia*

- **A total of 147 participants were randomly divided into three groups, taking 25 mg/day of ergothioneine, 10 mg/day of ergothioneine, or a placebo.**
- **After 16 weeks of treatment, cognitive function was assessed.**

Results

- **Reaction time**

Compared to the control group, participants who took 10 mg and 25 mg of ergothioneine had significantly shorter reaction times when performing the same tasks

- **Cognition**

Both groups taking ergothioneine showed significant improvements in cognitive domains such as executive function, complex attention, cognitive flexibility, and verbal memory.

- **Sleep**

Individuals taking 25 mg/day of ergothioneine had significantly higher sleep scores, indicating that ergothioneine can improve sleep quality.

Examples of products

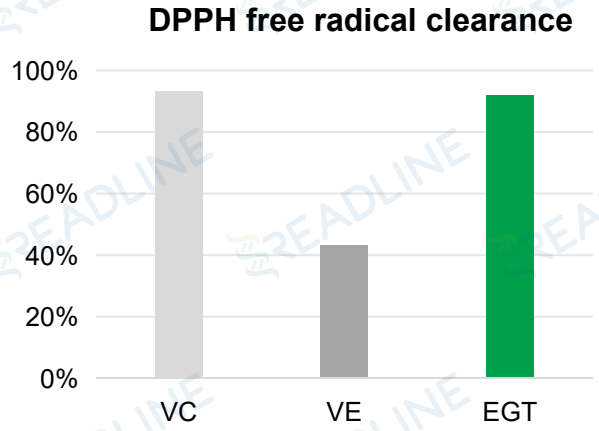
Claimed Efficacy:

- Brain fuel, enhances concentration, memory
- Promotes longevity and healthy aging
- Improves cognitive function and heart health
- Natural antioxidant
- Support cell energy, anti-oxidation, anti-aging

Examples of products: ergothioneine content

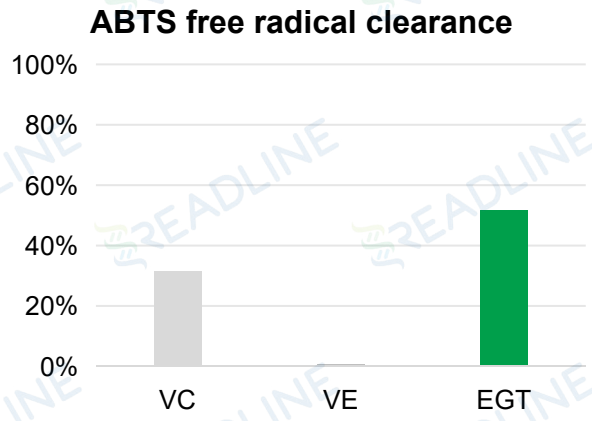
Brand & Product Name	Ergothioneine Content	Claimed Efficacy
Swisse L-ERGOTHIONEINE HA COLLAGEN+	5 mg / 3 capsule	Precise Repair, Lifting and Firming
LIFE EXTENSION Essential Youth L-Ergothioneine	5 mg / capsule	Expel Free Radicals, Revitalize Skin, Maintain Youthfulness
WRIGHT LIFE EGT-Ergothioneine	15 mg / capsule	Brightening and Firming
GeneIII Ergothioneine capsule	25 mg / capsule	Boost Vitality and Blood Circulation, Improve Sleep, Delay Aging, Maintain Mitochondrial Health
MapleWell Ergothioneine capsule	30 mg / capsule	Age-Defying Beauty, Brightening and Firming, Boost Energy, Improve Sleep
Yiayeah / Chstarina EGT1500	50 mg / capsule	Empower Cells, Rejuvenate Body, Enhance Sleep Quality

Comparison of antioxidant capability of ergothioneine, vitamin C, vitamin E



1000 ppm ergothioneine (EGT), vitamin C (VC) and vitamin E (VE) were reacted with DPPH for 30 min, and the optical density at 420 nm was recorded.

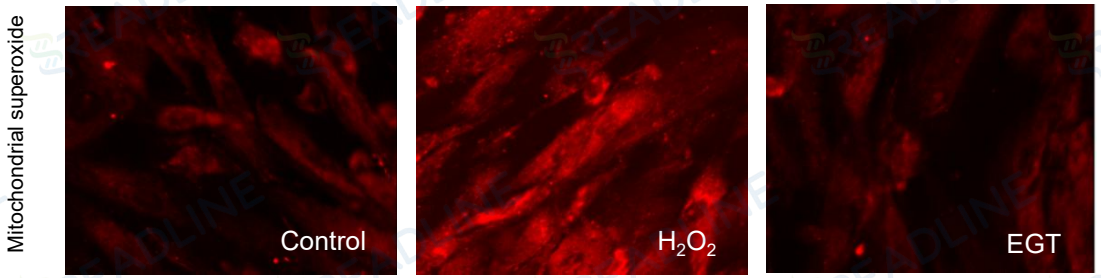
DPPH free radical solution shows a purple colour. When free radicals are eliminated, the colour fades away.

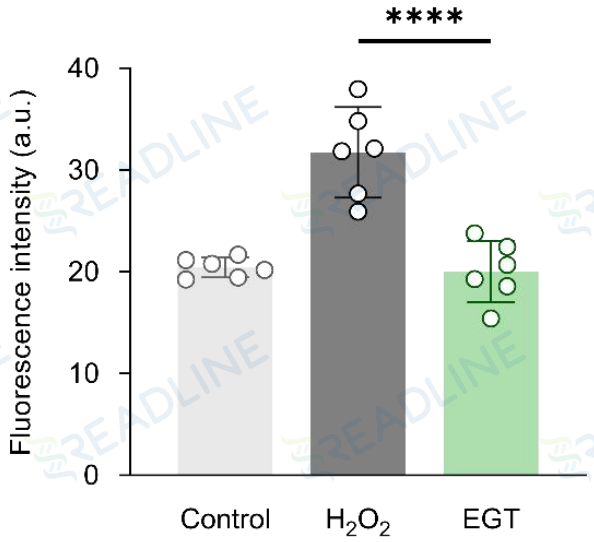


1000 ppm ergothioneine (EGT), vitamin C (VC) and vitamin E (VE) were reacted with ABTS for 5min, and the optical density at 517 nm was recorded.

Ergothioneine shows better capability of radical clearance than VC and VE

Ergothioneine can improve mitochondrial function

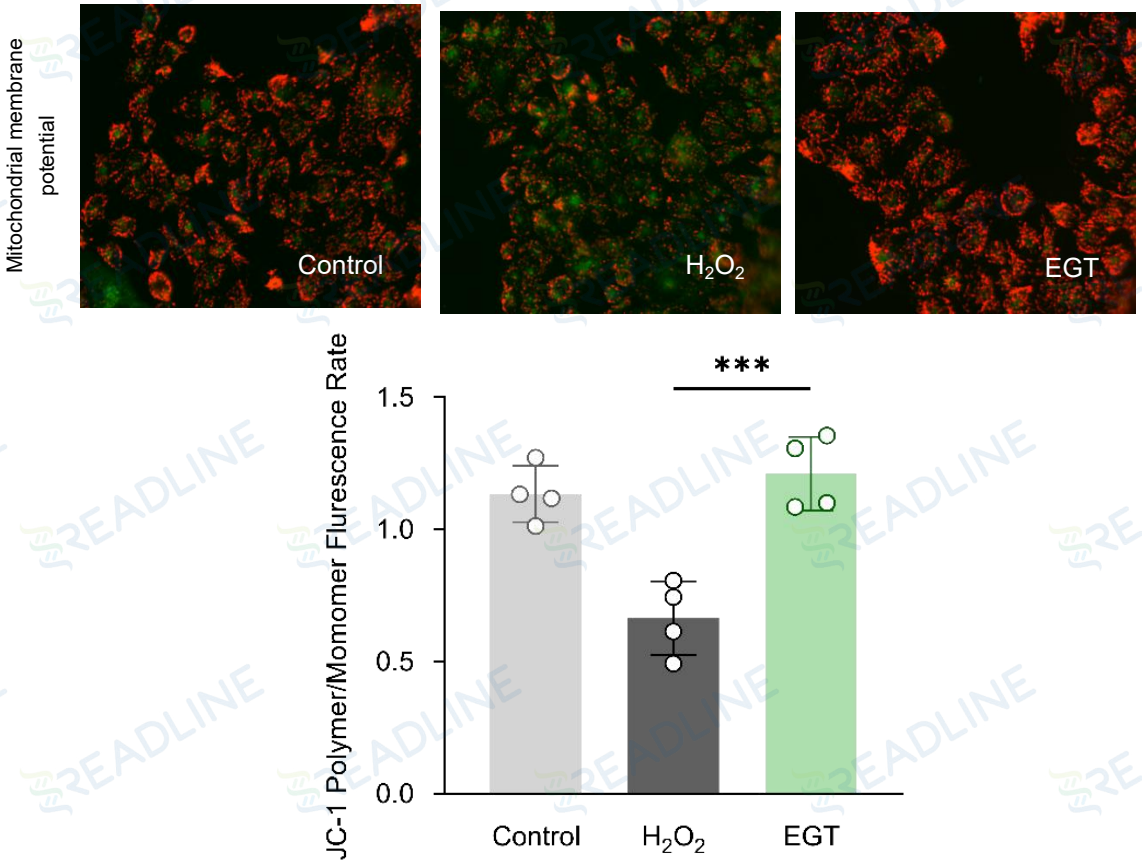




Reduce the mitochondrial superoxides

- HFF-1 cells were incubated with 500 ppm ergothioneine (EGT) for 24 h and then stimulated with 800 μM hydrogen peroxide for 1.5 h, MitoSox Red superoxide indicator was incubated in the incubator for 30min to analyze the fluorescence intensity of mitochondrial superoxide (λ_{ex} = 396 λ_{em} = 610).

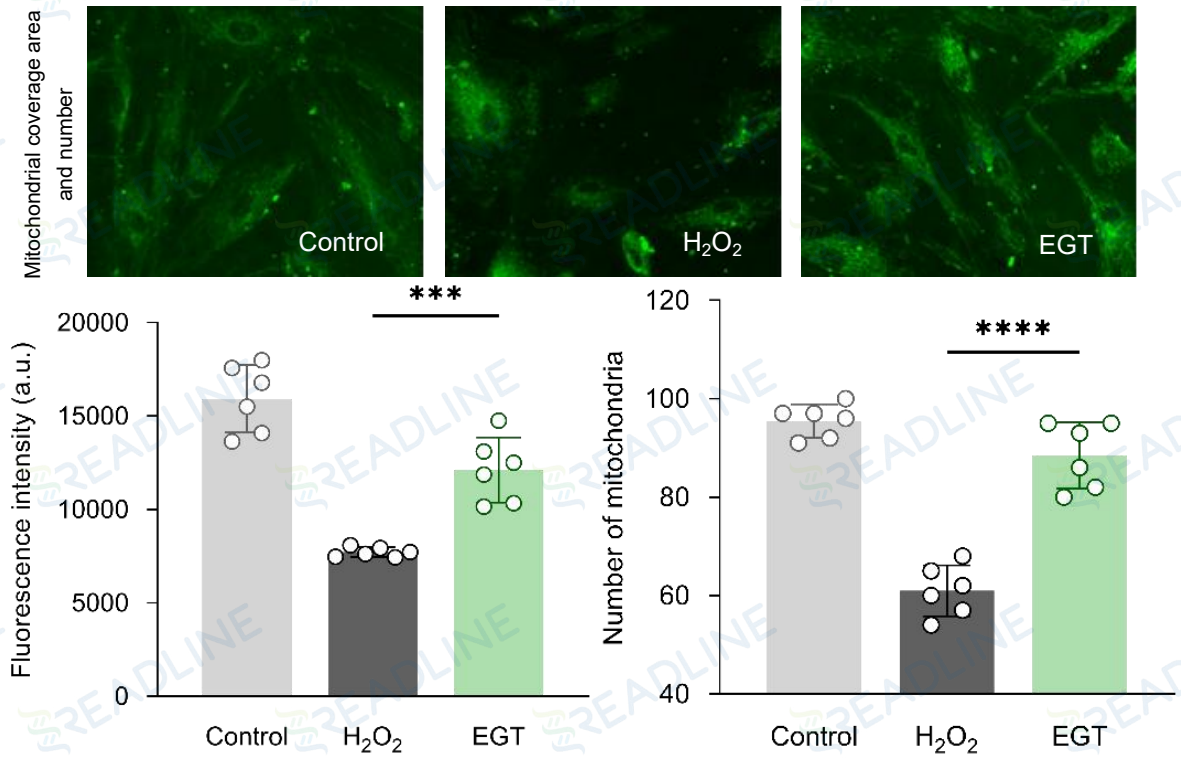
Ergothioneine can improve mitochondrial function



Maintain the mitochondrial membrane potential

- HaCaT cells were incubated with 500 ppm ergothioneine (EGT) for 24 h and then stimulated with 450 μM hydrogen peroxide for 1 h, JC-1 mitochondrial membrane potential fluorescence probe was added, incubated in the incubator for 30min, and the changes of mitochondrial membrane potential were analyzed by fluorescence microscopy (λex = 514 λem = 529).

Ergothioneine can improve mitochondrial function

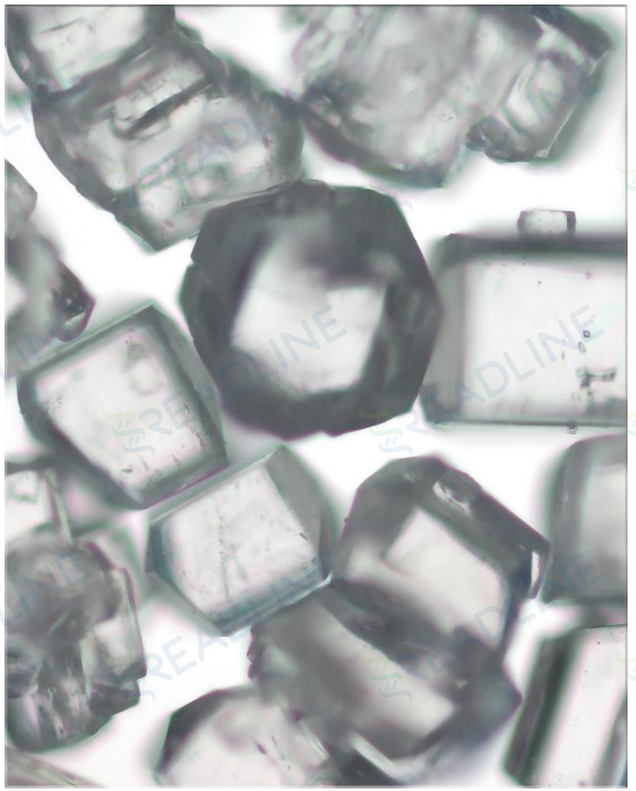


Maintain the quantity of mitochondria in cells

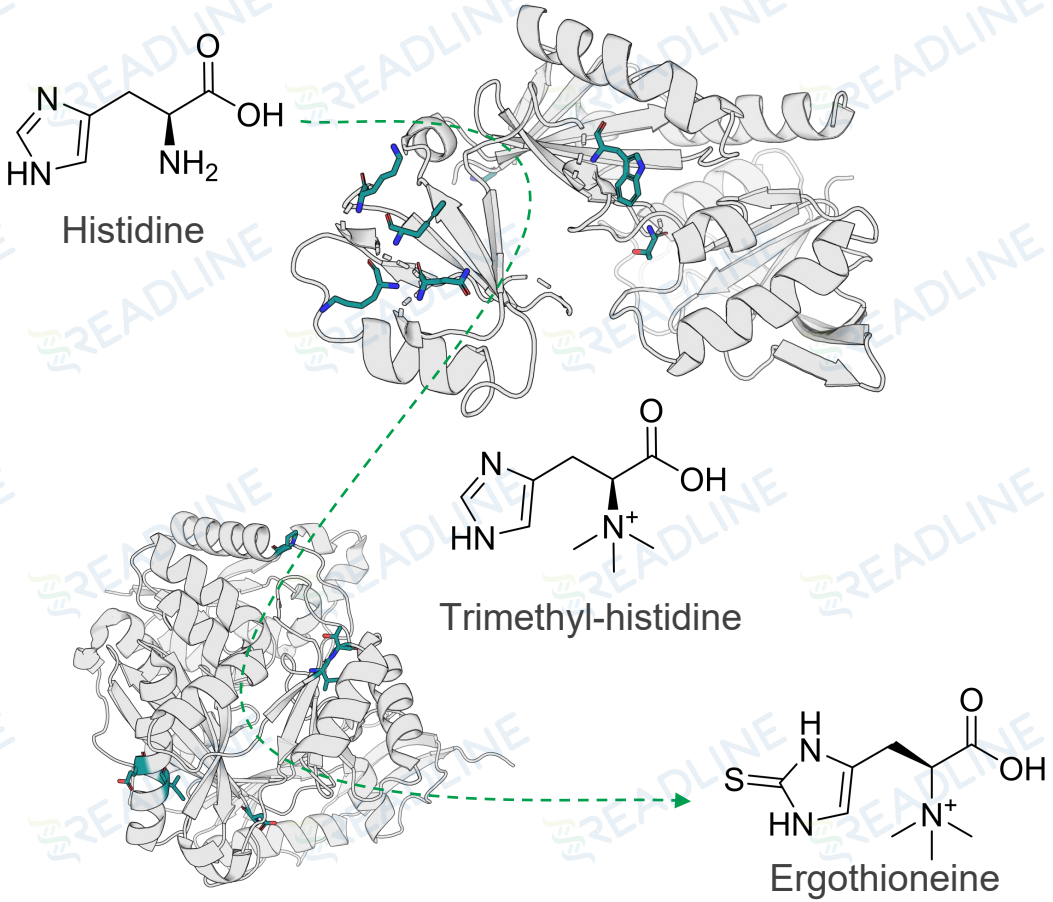
- HFF-1 cells were incubated with 500 ppm ergothionein (EGT) for 24 h and then stimulated with 800 μM hydrogen peroxide for 1.5 h, MitoTracker Green FM mitochondrial green fluorescence probe reagent was added, incubated in the incubator for 30min, and the mitochondrial morphological changes were analyzed by fluorescence microscopy (λex = 490 λem = 516).

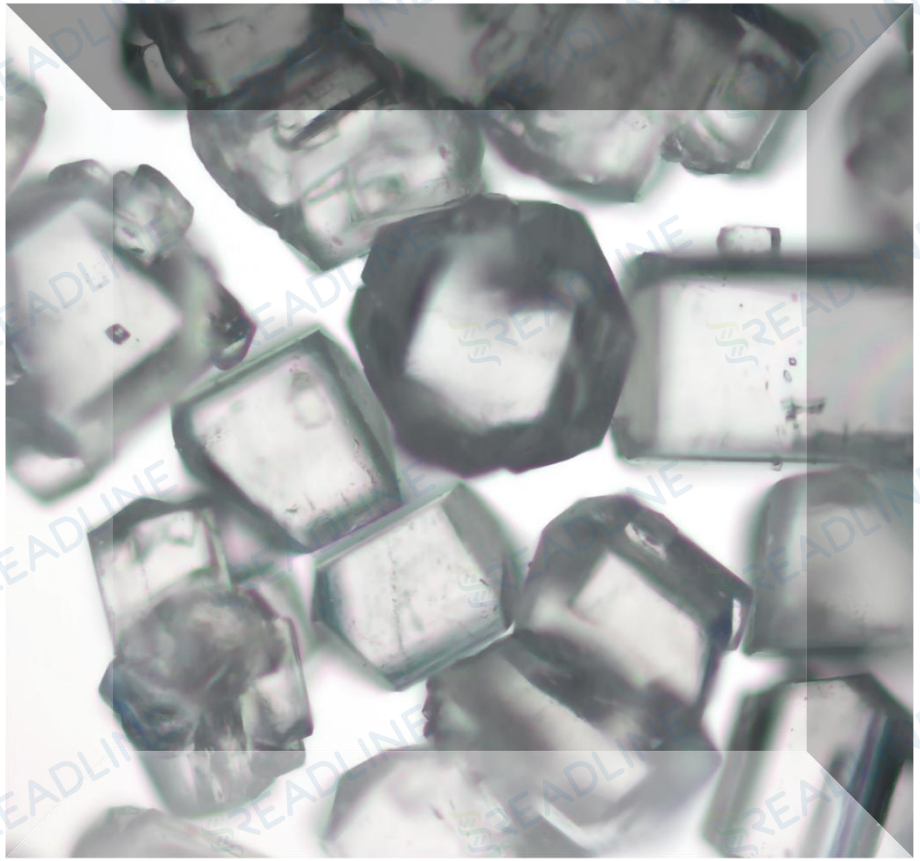
Readline ergothioneine: Compound Enzyme-Catalyzed Synthesis

Plant extraction	Chemical synthesis	Microbial fermentation	Readline: Compound Enzyme-Catalyzed



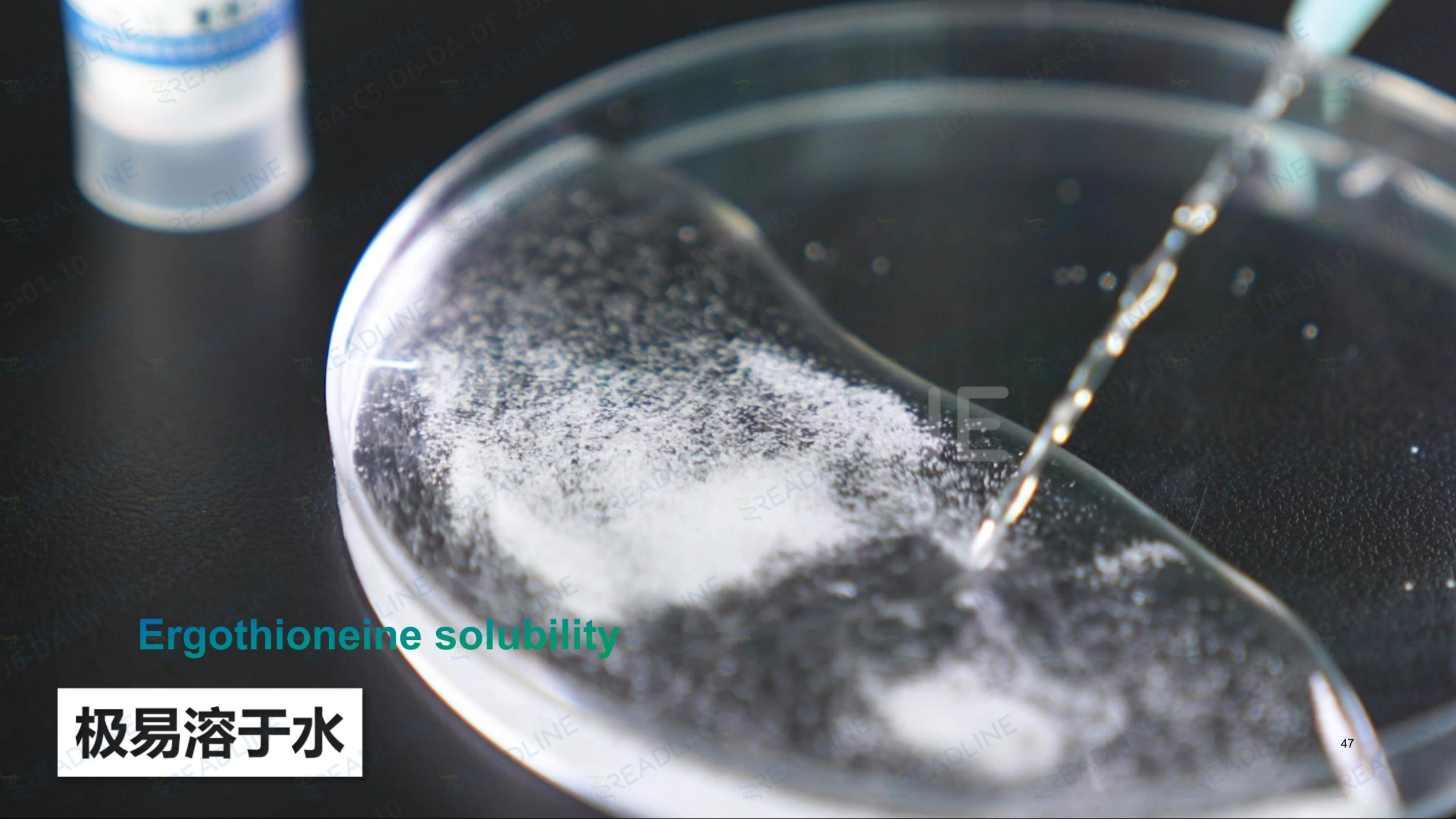
Readline Ergothioneine: Compound Enzyme-Catalyzed Synthesis





Readline Ergothioneine: high purity, high assay

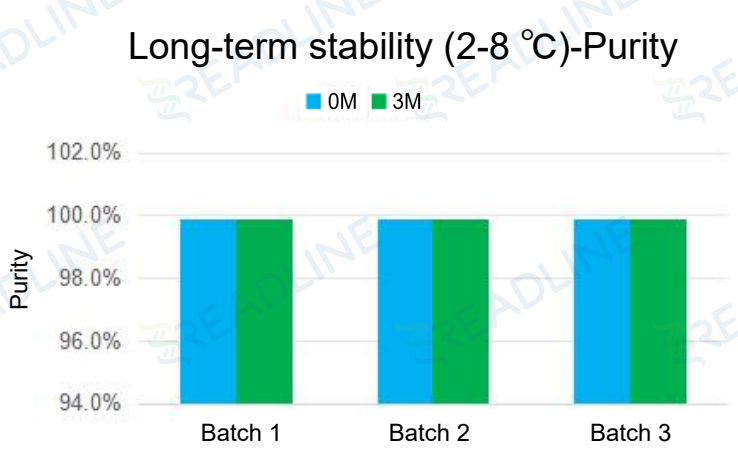
	Product A	Product B	Product C	Product D	Readline
Appearance					
Characteristics	White crystal	White crystal	White crystal	White powder	White crystal
Purity（%）	99.55	99.82	99.85	99.79	99.90
Assay（%）	98.69	99.08	99.13	98.87	100.3
Degree of specific rotation [α]D≥(+)122°（*c*=1）	127.9	126.3	125.9	127.1	126.8
Electrical conductivity（μs/cm）	10.3	7.11	1.4	18.8	1.5

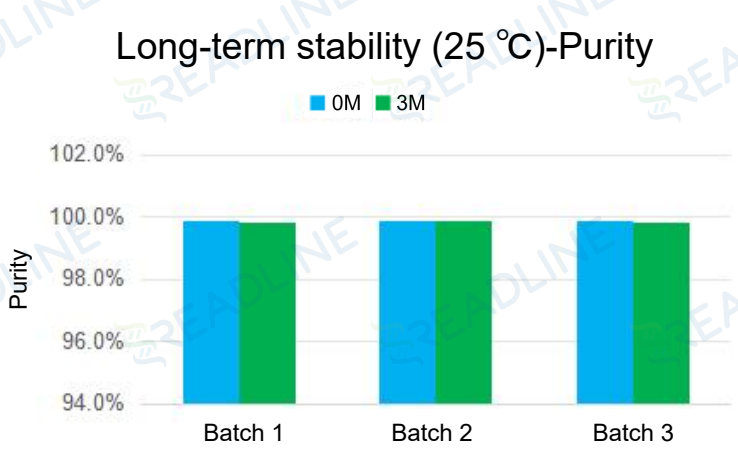


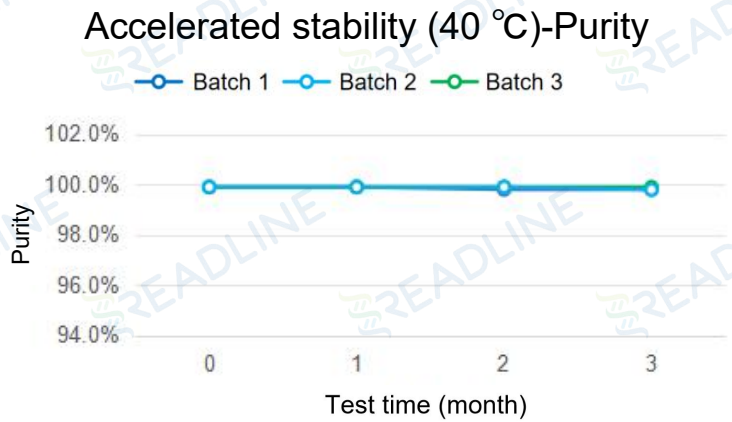
Ergothioneine solubility

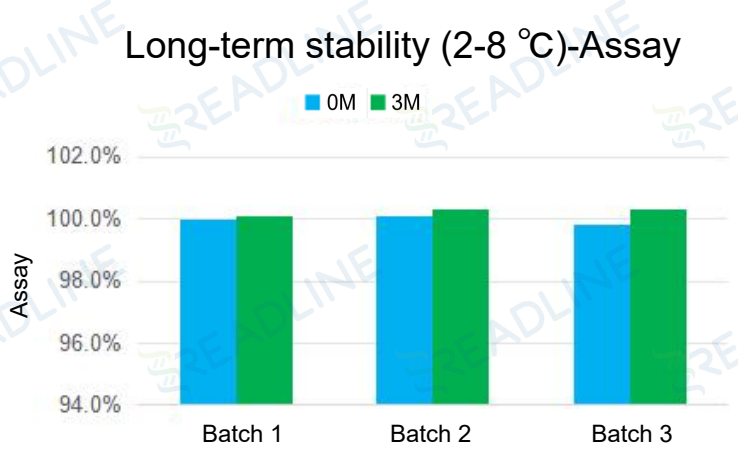
极易溶于水

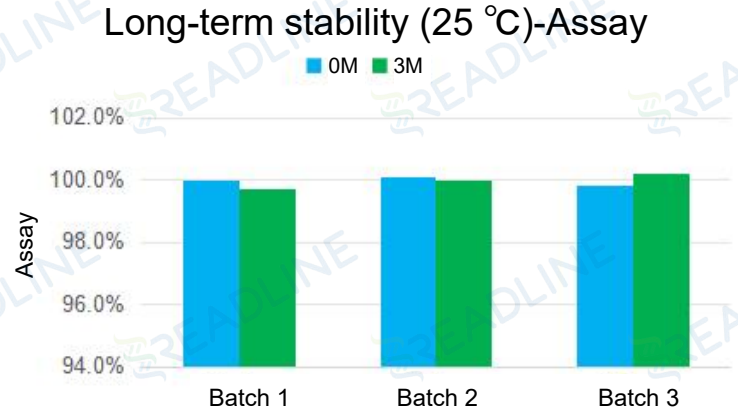
Readline Ergothioneine: high stability

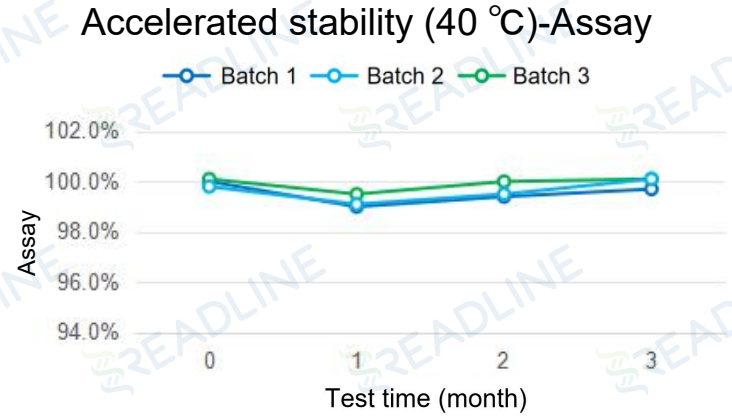










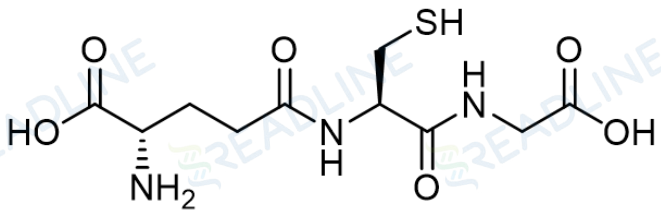


03

L-Glutathione Reduced

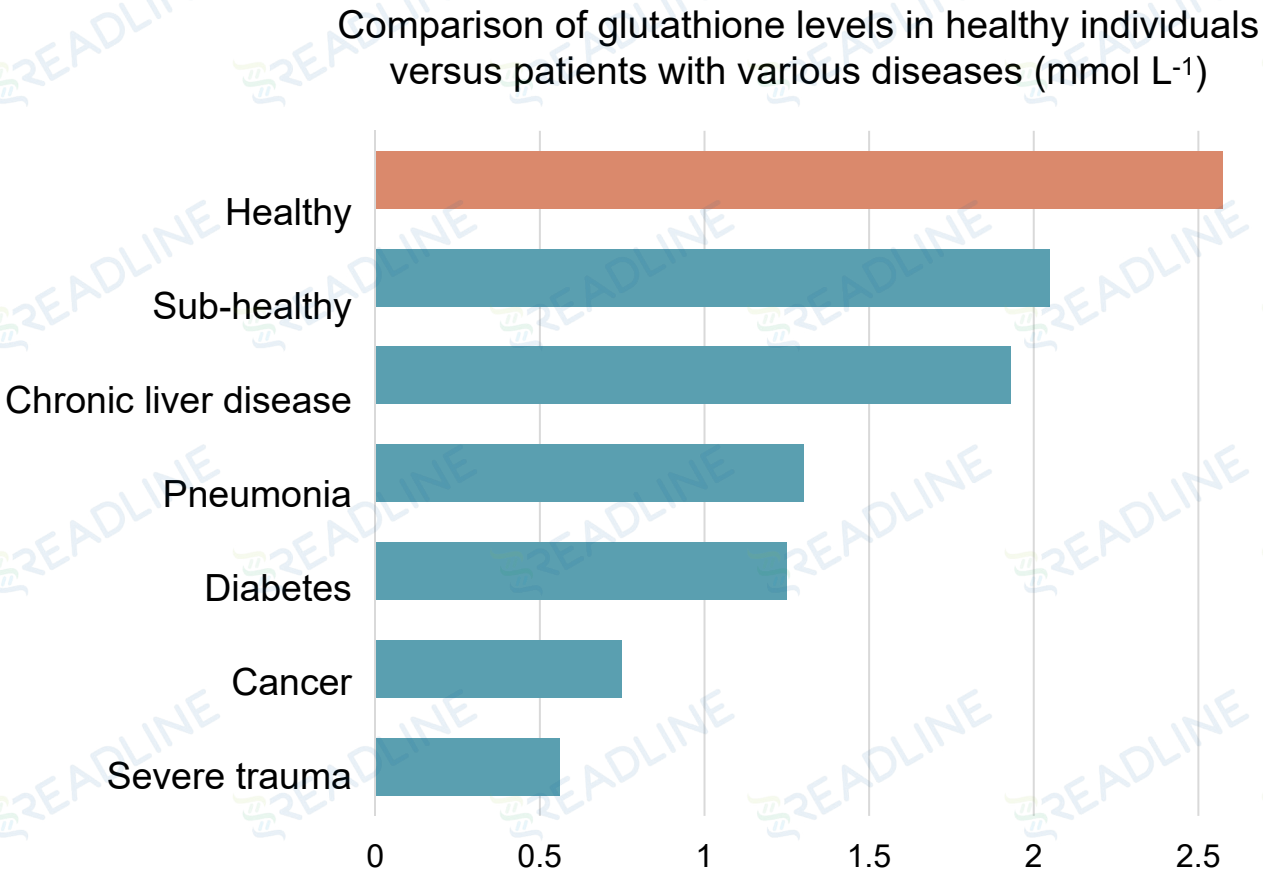
Product information

- **Product name:** L-Glutathione Reduced
- **Common name:** GSH
- **Recommended dosage:** 500 mg /day
- **CAS No.:** 70-18-8
- **Molecular formula:** $C_{10}H_{17}N_3O_6S$
- **Molecular weight:** 307.3

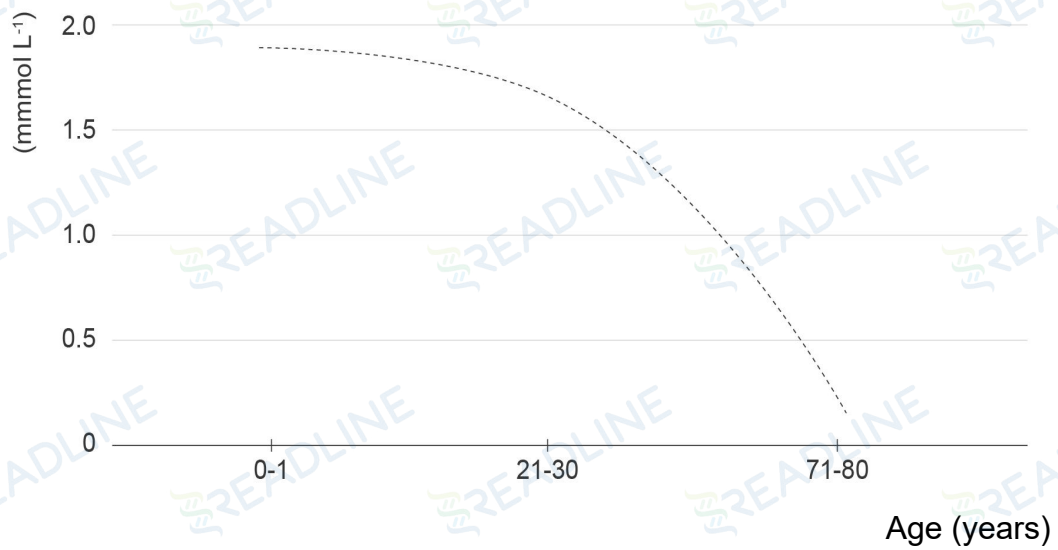


READLINE

Glutathione level decrease due to illness and aging

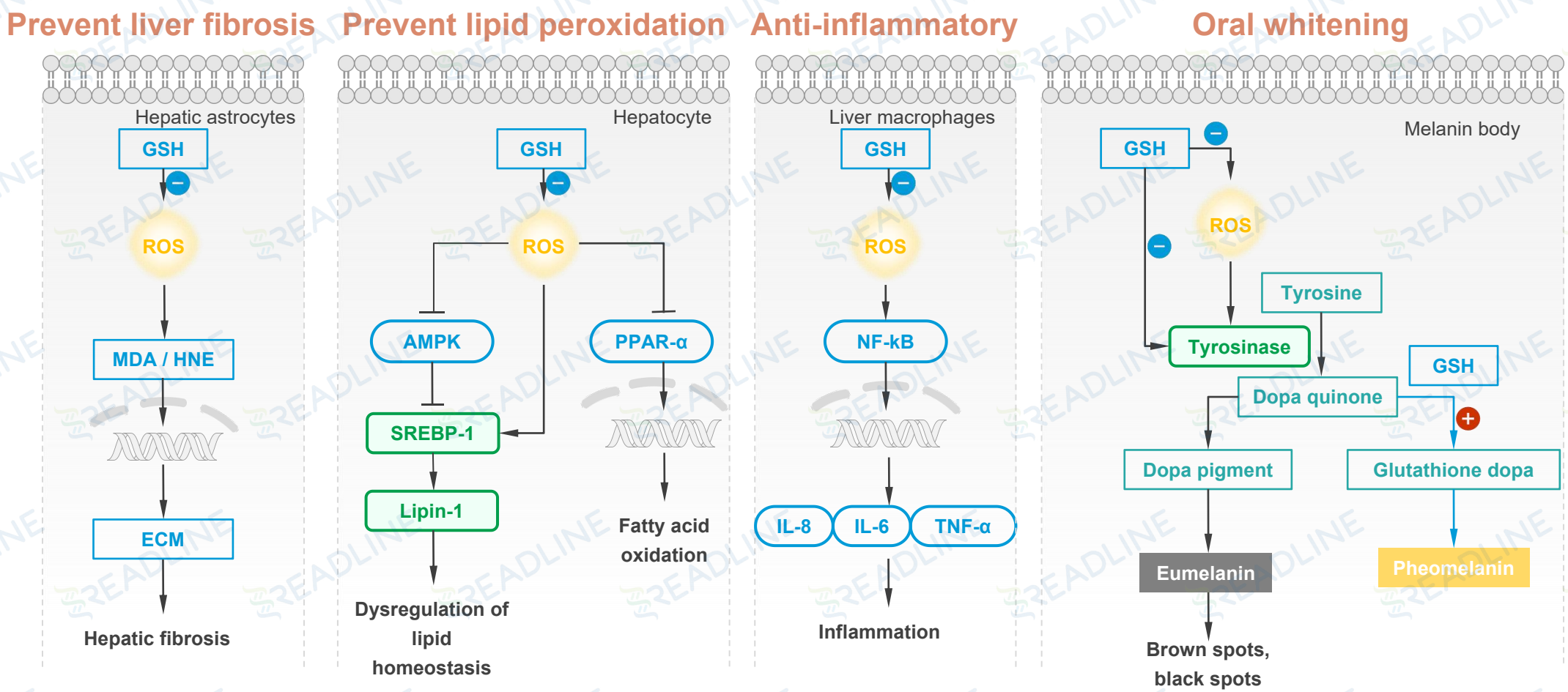


Glutathione in the human body gradually decreases with age, especially after the age of 25, and it needs to be supplemented constantly!



P. Kumar et al., *CLIN TRANSL MED.*, 2021,11, 372-353

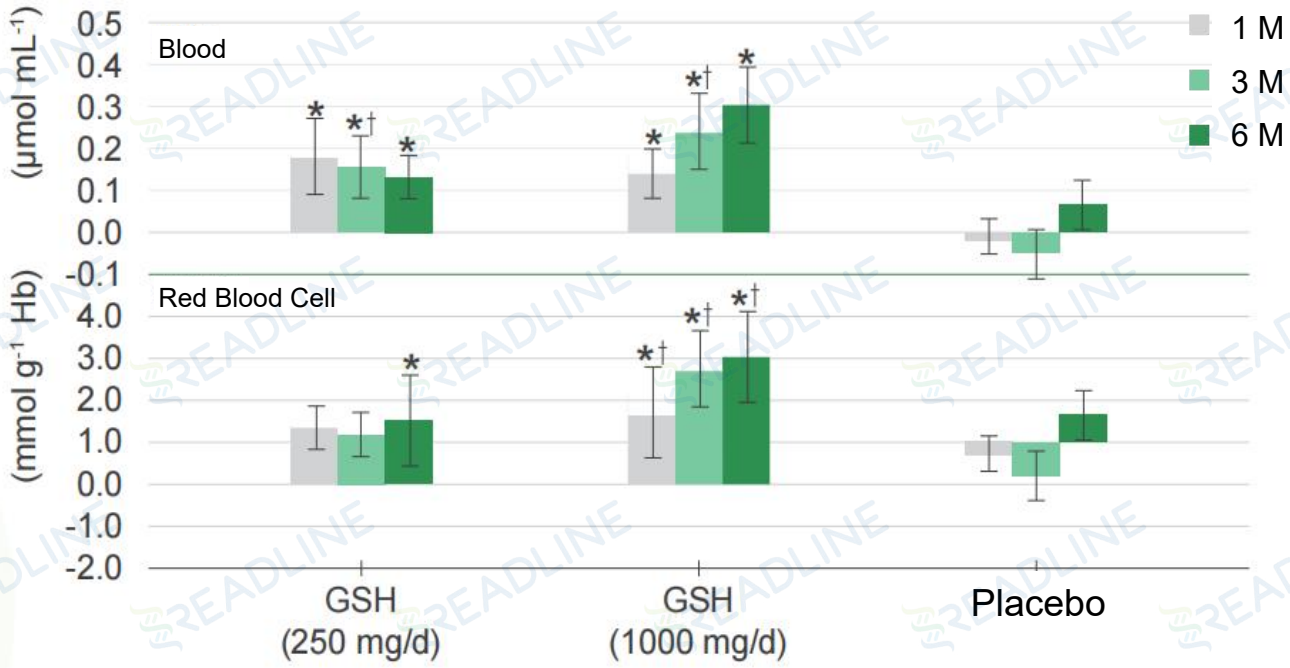
Mechanism: scavenging ROS (reactive oxygen species)



H. Ali et al., *Curr. Opin.* Toxicol., 2018, 1-8;E. Ceni et al., *WJG.*, 2014, 12, 21, 47, 17756-17772;H. J. Wang et al., *Annu. Rev. Nutr.*, 2012, 32, 11, 1–26

Effectiveness: glutathione level in human body can be increased when taken orally

The content of glutathione in human blood and red blood cells changes after oral administration of glutathione

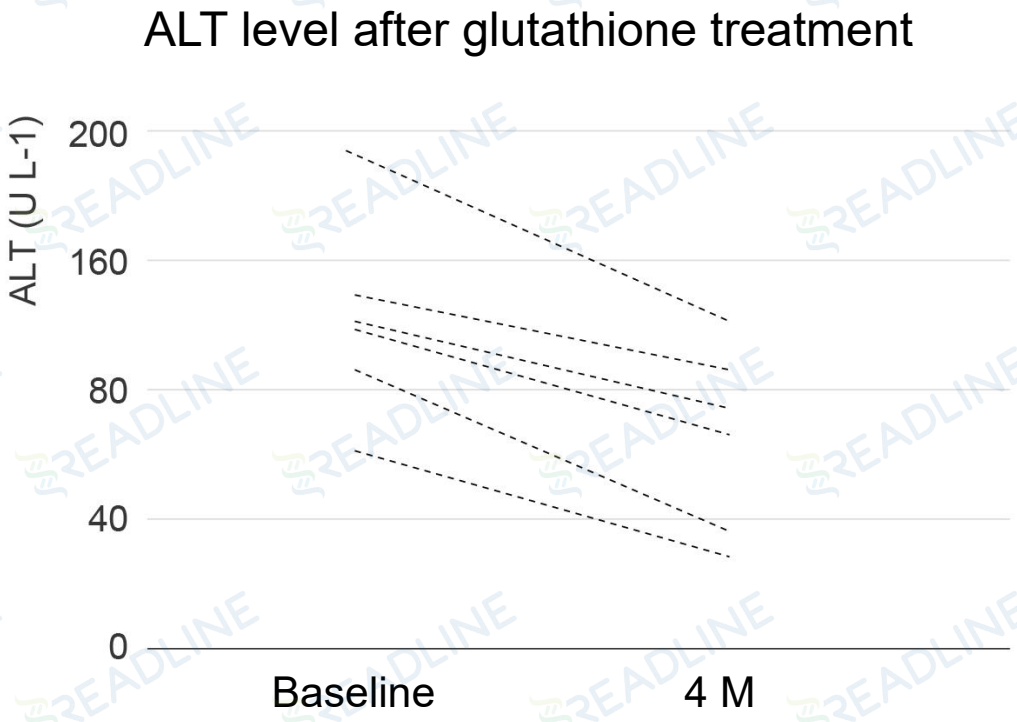


Description: Fifty-four healthy volunteers were given either a low dose (25 mg per day) or a high dose (1000 mg per day) of glutathione. Glutathione levels in human blood and red blood cells were monitored within 6 months of ingestion.

Results: The content of glutathione in human blood and red blood cells increased significantly after 1 month of glutathione intake, and no obvious adverse reactions were observed.

O. P. Richie Jr et al., *Eur J Nutr.*, 2015, 5, 52, 2, 251-263

Efficacy: Liver protection



Description:

15 patients with nonalcoholic fatty liver disease were supplemented with glutathione (300 mg/ day) and plasma ALT levels were measured after 4 months.

Results:

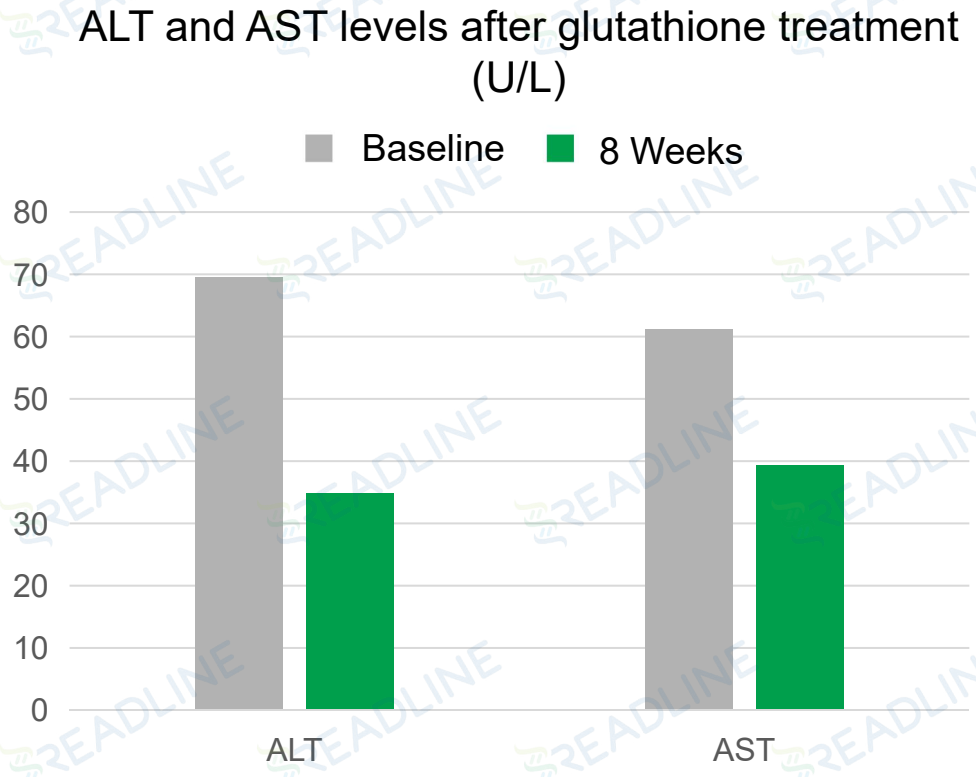
After glutathione treatment, the plasma ALT levels of all subjects decreased significantly.

Conclusion:

Glutathione can protect liver.

Honda et al., *BMC GASTROENTEROL.*, 2021,11, 372-353

Efficacy: Liver protection



Description:

The plasma levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were measured after 8 weeks of glutathione supplementation in 52 chronic hepatitis B patients (1200 mg/ day).

Results:

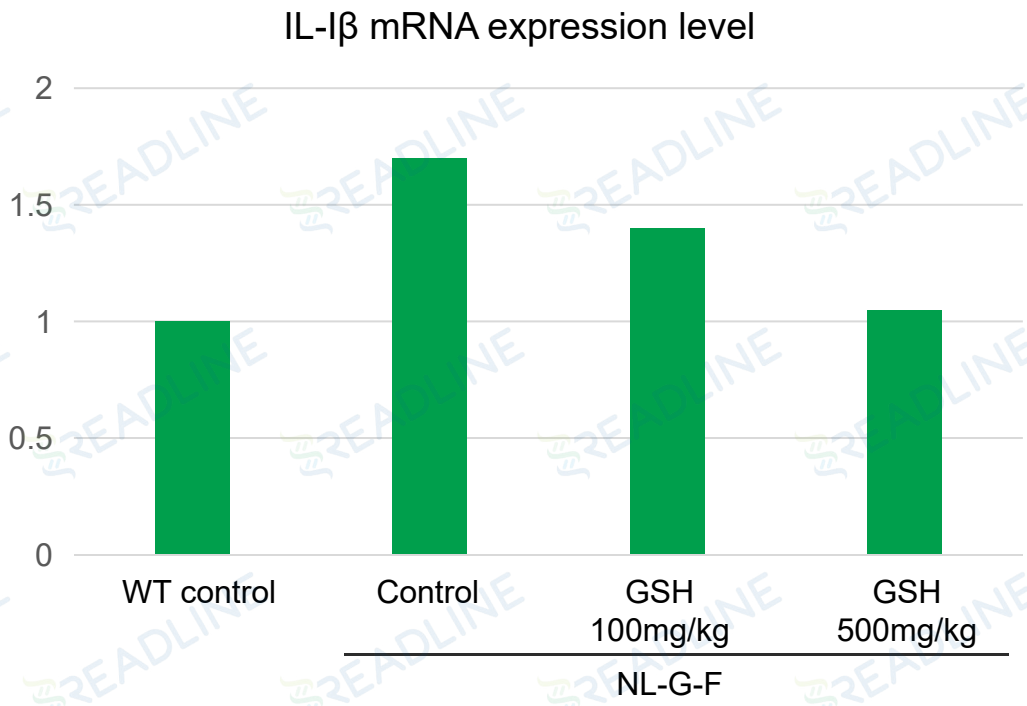
After glutathione treatment, plasma ALT and AST levels decreased significantly.

Conclusion:

Glutathione can protect liver.

Li Qian et al., *CENT EUR J IMMUNOL.*, 2017, 42, 97-100

Efficacy: improve immunity



Description:

12-month-old mice were divided into four groups, wild-type (WT) control and NL-G-F control were given distilled water daily, and the other two groups were supplemented with 100 mg/kg and 500 mg/kg of glutathione per day, respectively. After 21 days, the expression level of 1L-1β in the hippocampal region of mice was detected.

Results:

After glutathione supplementation, the expression level of 1L-1β in the hippocampal region of mice decreased significantly.

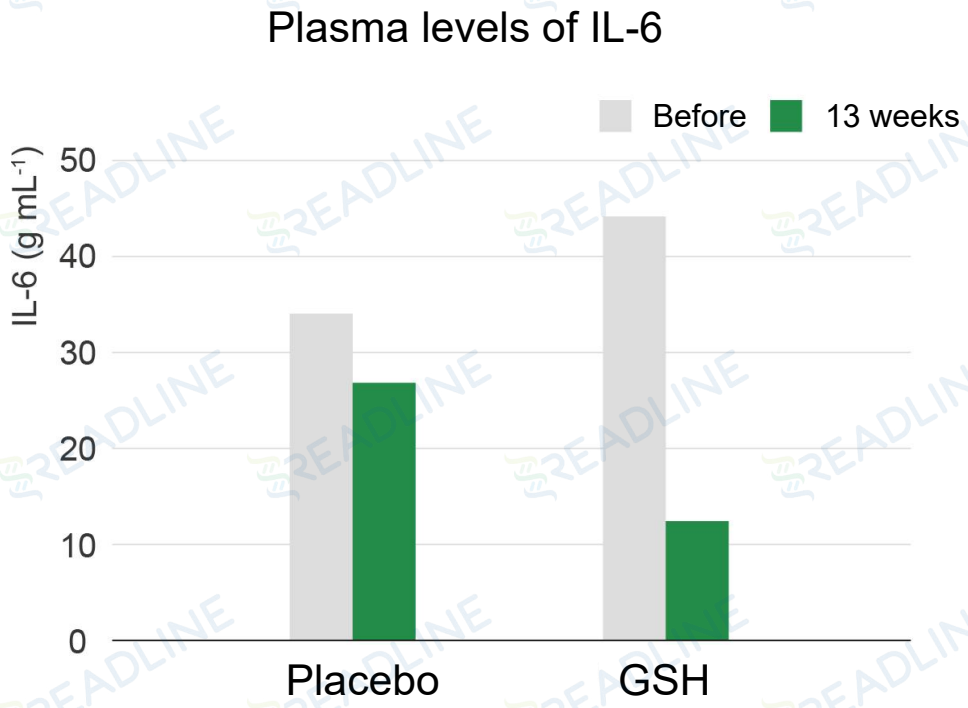
Conclusion:

Glutathione has anti-inflammatory effect.

READLINE

H. Izumi et al., *Neuropharmacology,* 2020,168, 108026

Efficacy: improve immunity



Description:

Fifteen HIV-positive patients were randomly divided into two groups, one of which was supplemented with glutathione (1260 mg/ day), and after 13 weeks, plasma levels of the inflammatory factor IL-6 were measured.

Results:

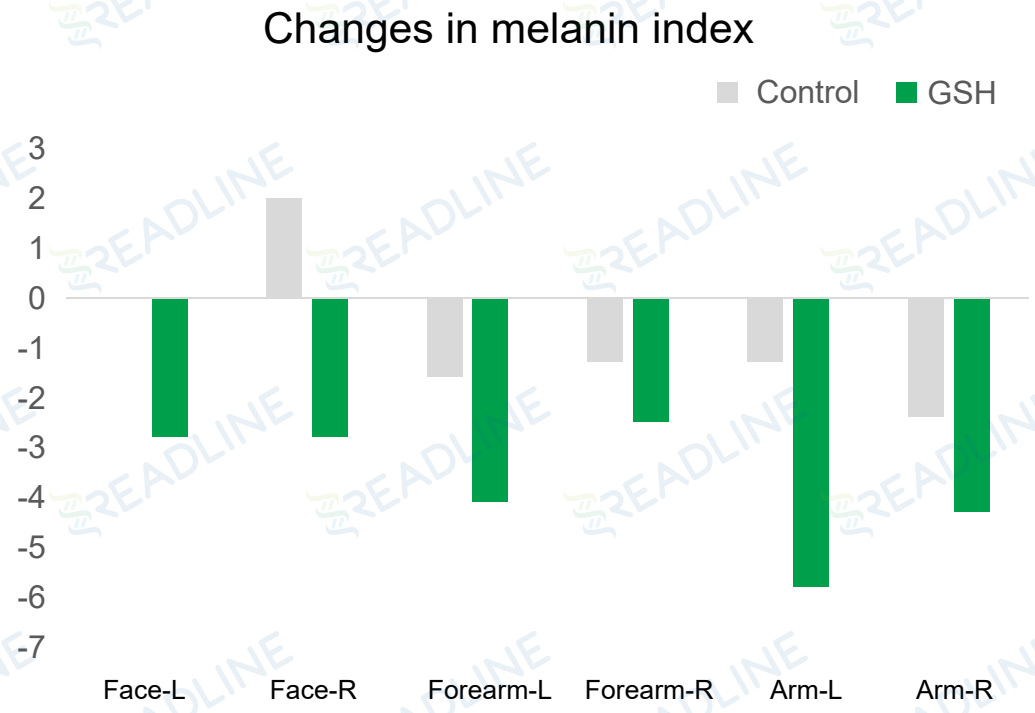
The plasma levels of the inflammatory factor IL-6 decreased significantly in subjects supplemented with glutathione.

Conclusion:

Glutathione can improve immunity.

Judy Ly et al., *J. Interferon Cytokine Res.*, 2015,11, 875-887

Efficacy study: oral skin-whitening



Description:

60 healthy subjects took glutathione orally at 500 mg/ day, and after four weeks, the melanin index in different parts of the subjects was measured.

Results:

Participants taking glutathione showed a decrease in melanin index measured at 6 different sites.

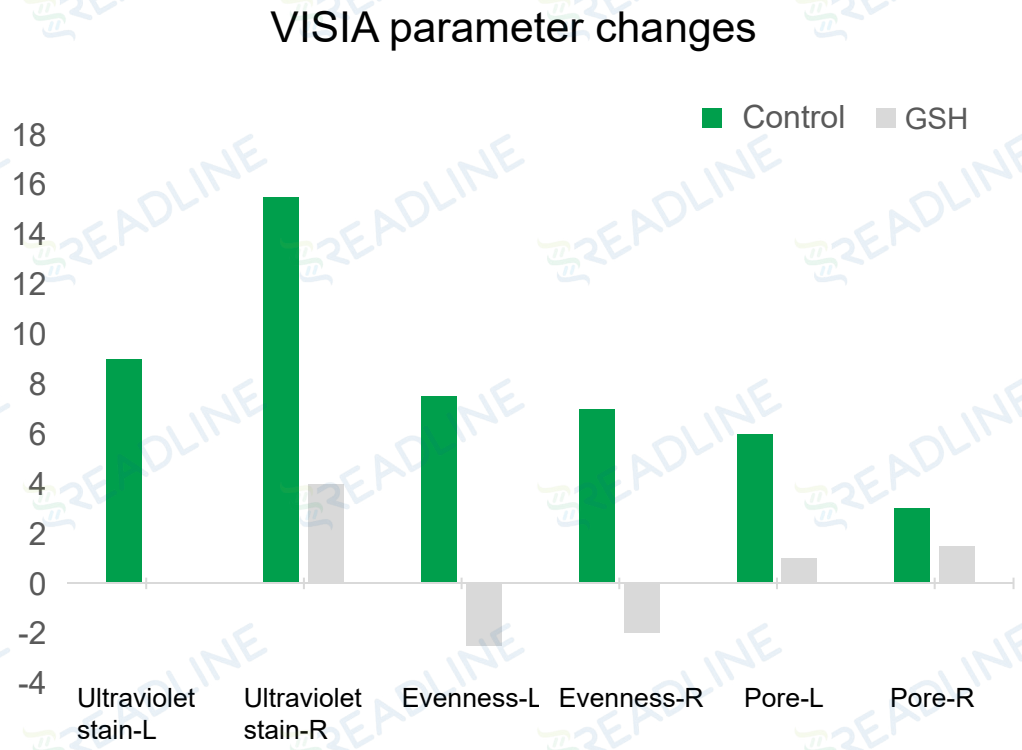
Conclusion:

Oral glutathione has whitening effect.

READLINE

J DERMATOL TREAT., 2012, 23, 97–102

Efficacy study: oral skin-whitening



Description:

60 healthy subjects took glutathione orally at 500 mg/ day, and after four weeks, VISIA parameters (stain, evenness, pore) in different parts of the subjects were measured.

Results:

The VISIA parameters measured at 6 different sites were decreased in the subjects taking glutathione.

Conclusion:

Oral glutathione has whitening effect.

J DERMATOL TREAT., 2012, 23, 97–102

Market applications of glutathione: health care

Product drawing					
brand	Healthy Origins	Jarrow Formulas	Starrhor	NOW	Codeage
place of origin	USA	USA	UK	USA	UK
Price	$41	$41	$45	$20	$56
specification	150 capsules/bottle	120 capsules/bottle	60 capsules/bottle	60 capsules/bottle	60 capsules/bottle
Dose /day	1 capsule	1 capsule	2 capsules	1 capsule	2 capsules
Glutathione content /capsule	500mg	500mg	500mg	250mg	250mg
Efficacy claim	Antioxidant Detoxification Improve immunity Protect skin	Antioxidant Detoxification	Antioxidant Boost immunity Increase fat Metabolism Detoxification Anti-aging	Antioxidant Boost immunity Detoxification	Antioxidant Boost immunity

Market applications of glutathione: oral skin-whitening

Brand	Picture	Glutathione content /capsule	Dose /day	Price
NENYEER		50 mg	2 capsules	$ 71.00
BECHI		50 mg	3 capsules	$ 66.00
Aokaco		200 mg	2 capsules	$ 71.00
Life extension		50 mg	1-3 capsules	$ 34.00
Vitahealth		20 mg	1 tablet	$ 55.00
Esmond Natural		200 mg	1 capsule	$ 71.00

Readline GSH: high quality

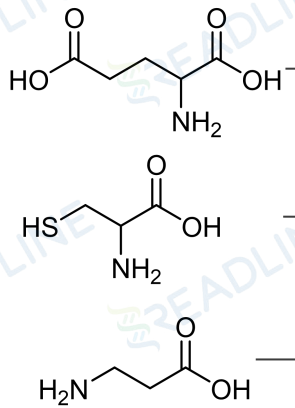
	Product A	Product B	Product C	Readline
Purity（%）	99.3	99.1	99.3	99.5
Assay（%）	99.0	99.3	99.1	100.3
Sulfate	≤300ppm	≤300ppm	≤300ppm	≤300ppm
Chloride	≤200ppm	≤200ppm	≤200ppm	≤200ppm
Ammonium salt	≤200ppm	≤200ppm	≤200ppm	≤200ppm
Optical activity	-16.8°	-17.4°	-16.4°	-16.5°
Drying loss (%)	0.3	0.3	0.4	0.1
Appearance	White powder	White powder	White powder	White crystalline powder

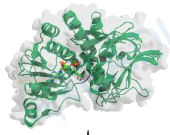
Readline GSH: patented enzymatic synthesis

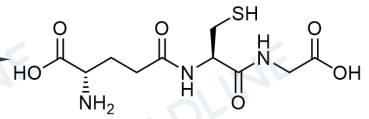
Glutamic acid

Cysteine

Glycine





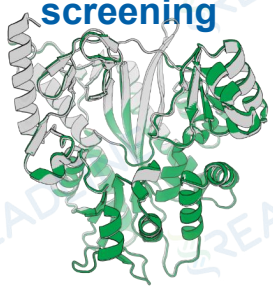


L-Glutathione Reduced

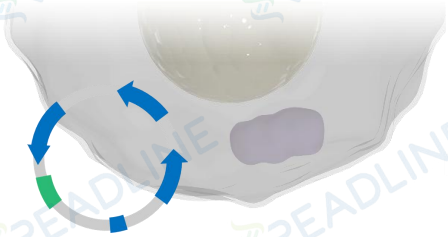
China patent：CN 111979206 B

New enzyme extraction

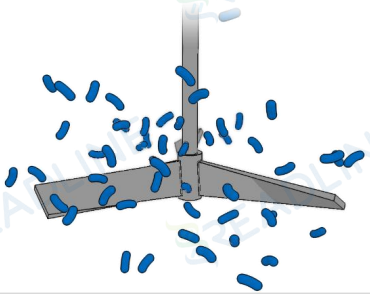
Enzyme modification and screening



Efficient expression

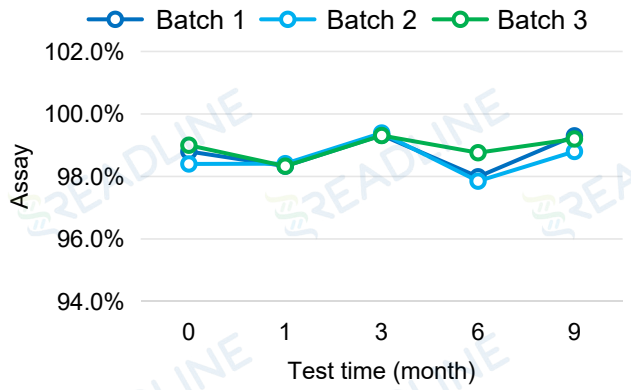


Enzymatic process

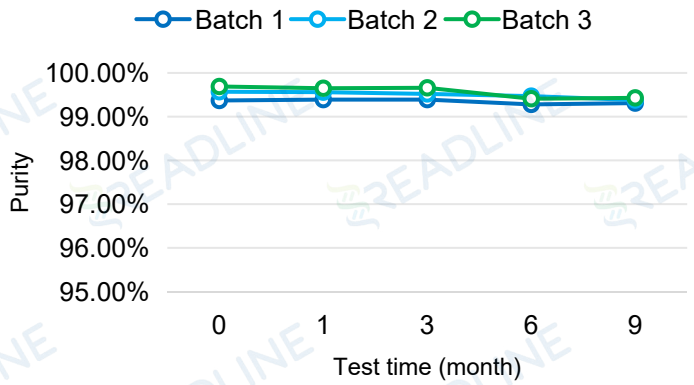


Product stability: accelerated test

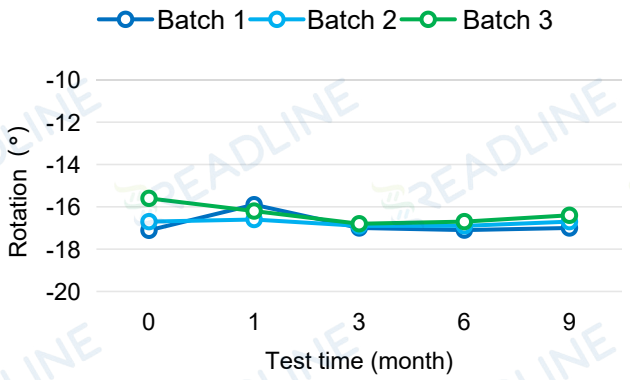
Accelerate stability (40 °C) assay



Accelerates stability (40 °C) purity

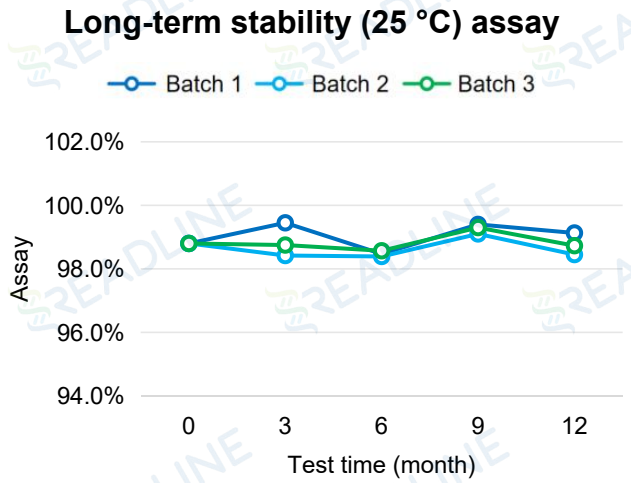


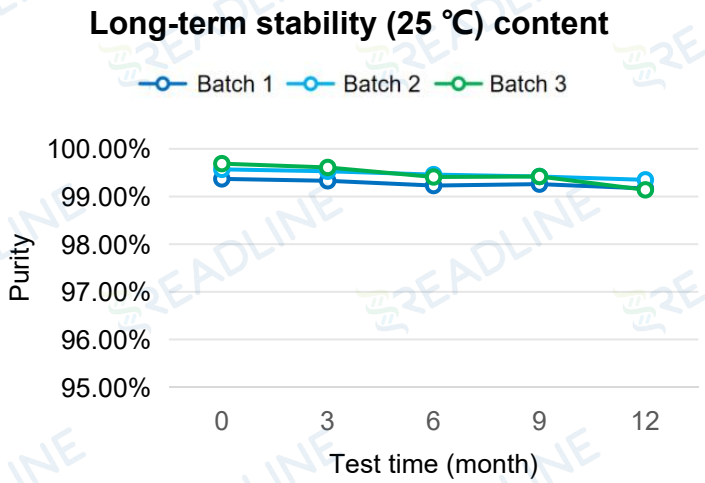
Acceleration stability (40 °C) by rotation

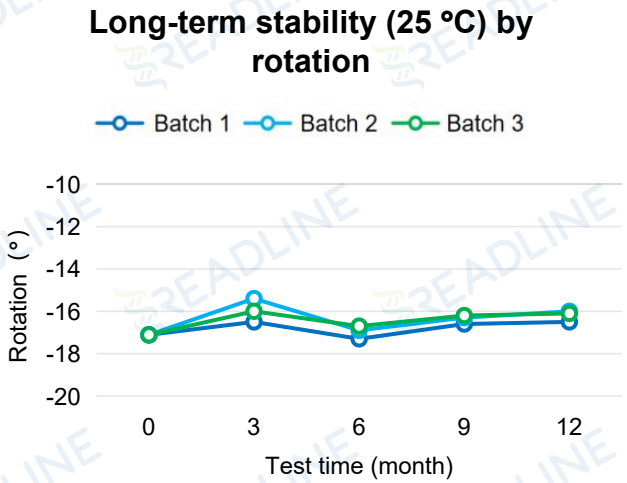


- **Conditions:** 40 °C, 270 days
- **Conclusion:** The glutathione powder was stable at 40 °C for 9 months, and the purity, assay and properties of glutathione powder did not change significantly

Product stability: long-term stability







- **Conditions:** 25 ℃, the investigation period was 12 months
- **Conclusions:** Glutathione powder was stable at 25 ℃ for 12 months, and the purity, assay and properties of glutathione powder did not change significantly

Product stability: package compatibility

Long-term storage of glutathione powder at 25 ℃ changes color

Test duration (month)	Aluminum foil	PE	PE+PE	PE+Aluminum foil
0	White powder	White powder	White powder	White powder
3	White powder	White powder	White powder	White powder
6	White powder	White powder	White powder	White powder
9	White powder	White powder	White powder	White powder
12	White powder	White powder	White powder	White powder

40 ℃ accelerated glutathione powder color change

Test duration (month)	Aluminum foil	PE	PE+PE	PE+Aluminum foil
0	White powder	White powder	White powder	White powder
1	White powder	White powder	White powder	White powder
3	White powder	White powder (caked)	White powder (caked)	White powder
6	White powder	Yellowish powder (caked)	Yellowish powder (caked)	White powder
9	White powder	Yellow powder (caked)	Yellow powder (caked)	White powder

READLINE

Green Active Ingredient Leader

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