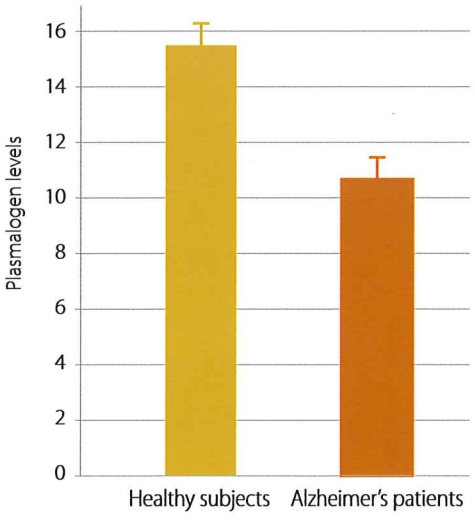
Scallop plasmalogen Explanatory leaflet

Plasmalogen is a natural component which exists in almost all tissues and accounts for about 18% of phospholipids in the body.
A study published in 1995 reported decreased levels of plasmalogen in the brains of Alzheimer's patients (brains of deceased patients). Subsequently, Team of professor Takehiko Fujino (Emeritus professor at Kyushu University) and a team in Canada confirmed that levels of plasmalogen were also clearly decreasing in the blood of living patients.
Research suggests that supplementation of this reduced plasmalogen is the key to improving dementia. Research and development of scallop-derived plasmalogen has been conducted by Takehiko Fujino and his team and clinical research thus far indicates that it is effective in the prevention and improvement of dementia.

Reduction of plasmalogen in the brains (hippocampus) of Alzheimer's patients



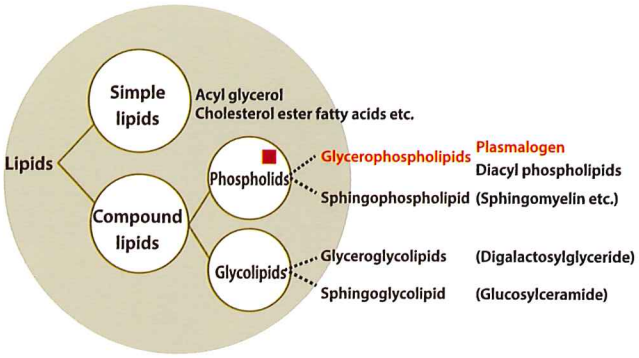
Guan Z et al. J Neuropathol Exp Neurol. 58, 740-747 (1999)

1 Basics of [Plasmalogen]

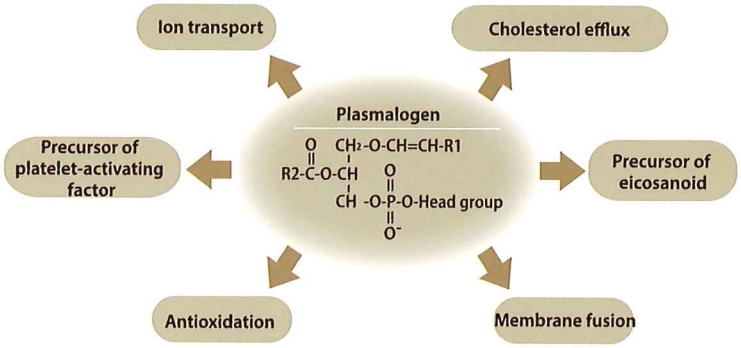
Plasmalogen is a type of **phospholipid with an antioxidant action**, and is one of the glycerophospholipids. Plasmalogen exists in all tissues of mammals and **accounts for about 18%** of human phospholipids. Particularly high levels are found in brain neurons, cardiac muscle, lymphocytes, and macrophages etc.

Among the various functions of plasmalogen known to date, the most well-known is its antioxidant function and when a cell undergoes oxidative stress, it is thought that plasmalogen displays the greatest defense function. Plamalogen is also involved in the **important ion transport across cell membranes**. Additionally, it is known to play an extremely important role in cell membrane fusion, namely the fusion of various cell membranes in brain cells, as well as **a role in the efflux of cholesterol and functions as a precursor of neurotransmitters**.

[Classification of lipids and plasmalogen]



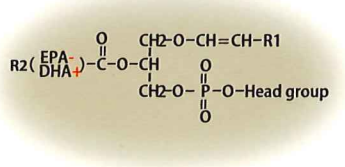
[Role of plasmalogen in the brain]



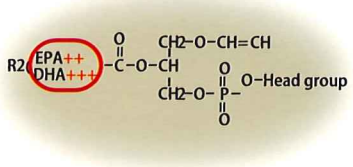
2 Development of scallop-derived plasmalogen

The raw material of plasmalogen was originally derived from chickens. However, as a result of subsequent research on various materials, the large scale extraction of scallop-derived plasmalogen, which is thought to be more effective in humans, **was achieved for the first time**. When compared with chicken-derived plasmalogen, scallop-derived plasmalogen was shown to **contain EPA** which chicken-derived plasmalogen does not, and to contain about **twice the amount of DHA**. This scallop-derived plasmalogen is being used in all the clinical trials currently being conducted.

[Chicken-derived]



[Scallop-derived]



* Japanese scallops are used, excluding the mid-gut gland which is said to contain heavy metals.

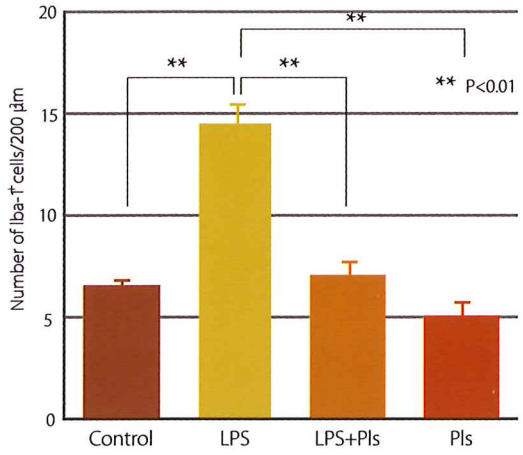
* Even if raw scallops are consumed in large quantities, levels of plasmalogen in the body do not increase efficiently. It is known that blood plasmalogen concentrations only begin to rise when specially extracted high purity plasmalogen is ingested.

Research data

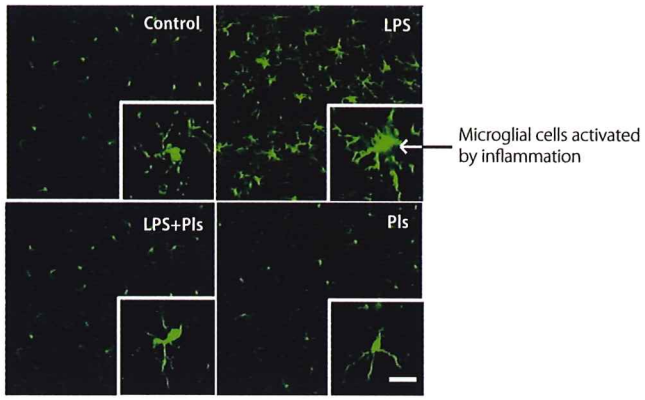
3 Basic research data

Anti-inflammatory effect on brain glial cells ①

Anti-inflammatory effect of plasmalogen (Pls) on brain nerve inflammation due to LPS (bacterial toxin) in the cerebral cortex (mouse).



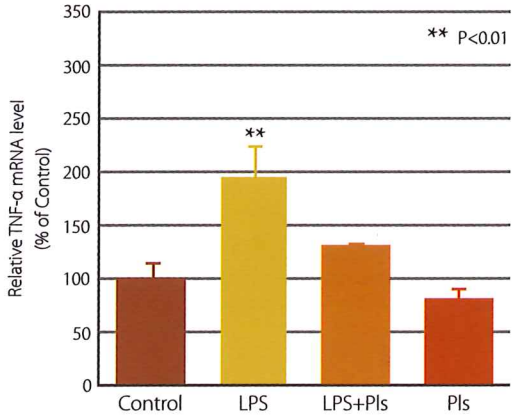
*Iba-1^{+} : Proteins specifically expressed in microglia etc.



Journal of Neuroinflammation 2012,9:197

Anti-inflammatory effect on brain glial cells ②

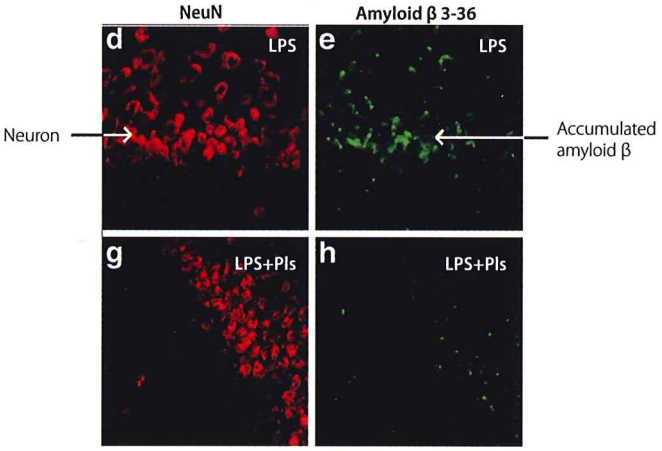
Inhibitory effect on production of inflammatory cytokines (TNF-α) in brain (mouse)



Journal of Neuroinflammation 2012,9:197

Inhibition of amyloid β protein accumulation

Inhibition of Aβ protein accumulation in the hippocampal CA_1 area due to LPS (bacterial toxin)

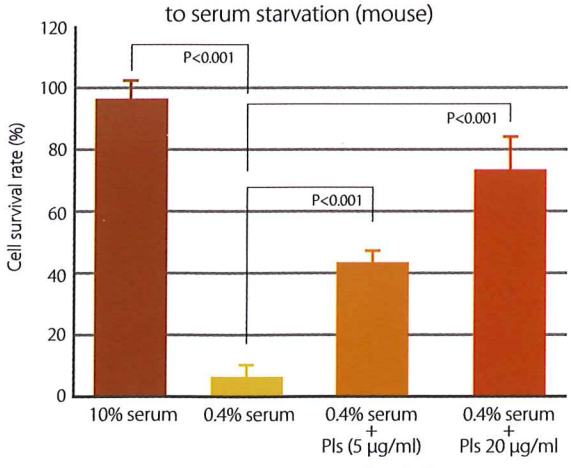


* NeuN: Neuronal Marker

Excerpt from Journal of Neuroinflammation 2012, 9:197

Anti-apoptotic effect

Inhibition of apotosis of Neuro-2A cells due to serum starvation (mouse)



PLos ONE 2013, 8: e83508

Decrease in LDL cholesterol

Reduction in blood LDL cholesterol levels in diabetic-obese mouse models (mouse) due to administration of plasmalogen

	Control diet (n=10)	PlsEtn diet (n=10)	t-test
Total chol (mg/100ml)	206.3±17.4	173.5±15.3	P<0.001
HDL-chol (mg/100ml)	60.3±14.1	57.5±9.6	
LDL-chol (mg/100ml)	9.2±4.4	5.1±2.4	P<0.02
TG (mg/100ml)	1267.4±367.9	1244.6±361.2	
Glucose (mg/100ml)	541.9±172.8	507.5±155.2	
Albumin (g/100ml)	4.6±0.3	4.5±0.3	
Body weight (g)	407.5±30.9	391.5±40.1	

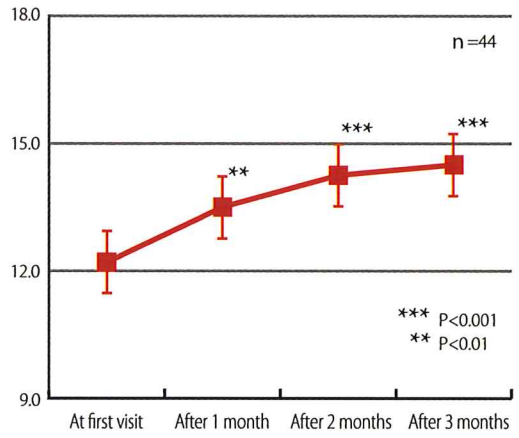
Excerpt from Lipids in Health and Disease 2012, 11:161

4 Clinical study data (Subjects with moderate or severe dementia Scallop-derived plasmalogen used)

* Source: Excerpt from an interim report of the double blind trial of the effect of plasmalogen-containing food on cognitive function in patients with mild Alzheimer's disease or mild cognitive impairment.

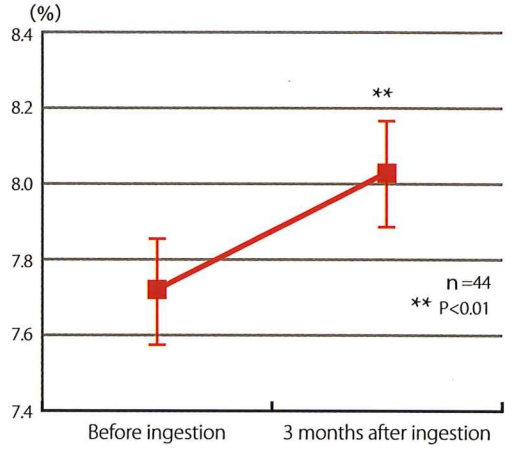
Improvement in MMSE score

Changes in MMSE score (cognitive function test)



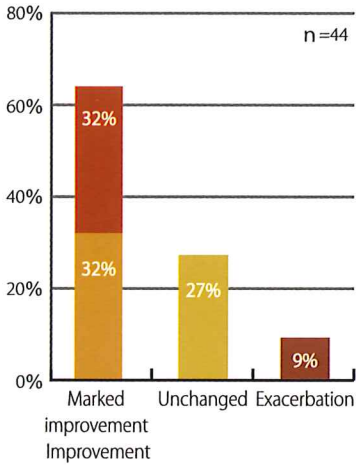
Change in blood concentration of PIs

Change in blood concentration of plasmalogen (PI-PE) due to ingestion



MMSE improvement rate

Improvement rate in MMSE test



Marked improvement = an increase of 4 points or more

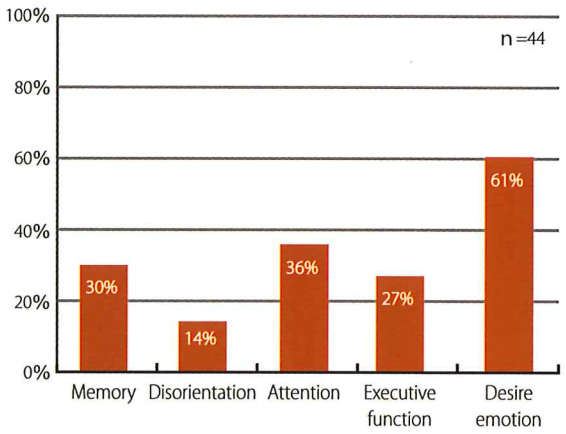
Improvement = an increase of 2 points or more

Unchanged = A change of less than 2 points ±

Exacerbation = a decrease of 2 points or more

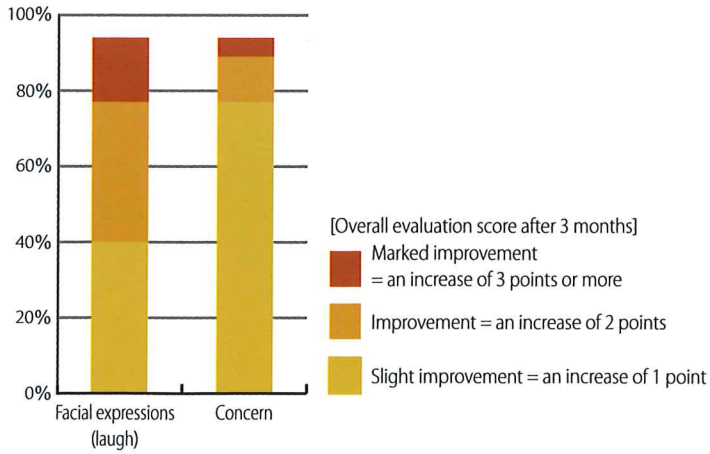
Improvement of core symptoms of dementia

Evaluation of each item after 3 months of ingestion by carers



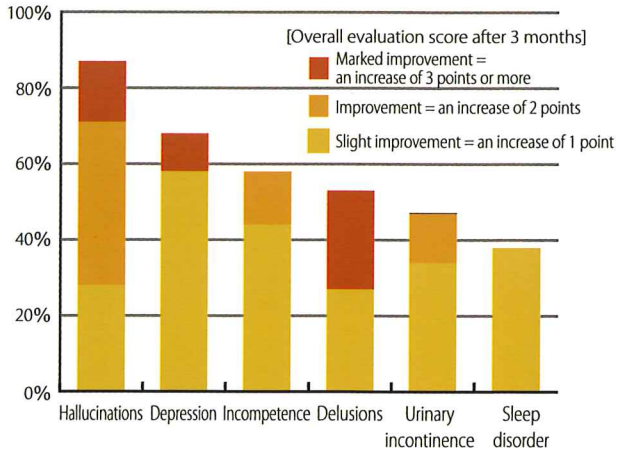
Improvement of peripheral symptoms ①

Improvement of peripheral symptoms of dementia according to objective evaluation by carers



Improvement of peripheral symptoms ②

Improvement of peripheral symptoms of dementia according to objective evaluation by carers



5 Role in the treatment and prevention of dementia.

Laboratory investigations conducted in the Faculty of Medical Sciences and Faculty of Science at Kyushu University and in the Institute of Rheological Functions of Food, suggest that Plasmalogen plays the following types of role in the treatment and prevention of dementia.

- **Anti-inflammatory and antioxidant actions**
- **Neurogenesis**
- **Enhances synaptic and neuron functions**
- **Inhibits accumulation of amyloid β**
- **Improves learning and memory functions**

6 Development history and clinical trials

2006: ● Discovery of a method to extract high purity plasmalogen from hens (Patent publication pending 2006-23296 Patent pending 2007-16056)

2007: ● Successful improvement and simplification of the plasmalogen detection method. (Paper 1: Analytical Biochemistry 370:54-59, 2007)

2009: ● Initiation of a case study on oral administration of "Plasmalogen" to Alzheimer dementia patients (ongoing).
The safety and improvement effect on human Alzheimer dementia was confirmed.

2012: ● Plasmalogen in erythrocytes of patients with Alzheimer's dementia was shown to be reduced.
(Paper 4: Dement Geriatr disord Extra 2:298-303, 2012)

● Administration of plasmalogen in animal models of Alzheimer dementia was shown to be effective.
(Inhibits brain nerve cell inflammation/ Inhibits accumulation of amyloid β proteins.)
(Paper 2: Journal of Neuroinflammation 9:197, 2012)

● Oral administration of plasmalogen was shown to increase erythrocyte plasmalogen.
(Paper 3: Lipids in Health and Disease 11:161-167, 2012)

● Safety studies on plasmalogen were completed.

2013: ● Plasmalogen was shown to inhibit apoptosis through the activation of Akt and ERK1/2.
(Paper 5: PLos ONE 2013, 8: e83508)

2014: ● Extraction of high purity plasmalogen from scallops was achieved. Safety studies were completed.
● Initiation of a double blind study of the effect of scallop-derived plasmalogen in food on patients with mild dementia (Alzheimer type).

2015: ● Initiation of an open-label study of the effect of scallop-derived plasmalogen in food on patients with moderate or severe Alzheimer's disease and other types of dementia.

2016: ● Plasmalogen was shown to activate Akt and ERK 1/2 via several orphan G protein-coupled receptors.
(Paper 6: PLos ONE. 2016, 11: e0150846)

■ Double blind study (number of confirmed subjects: 328)

Study title: Effect of plasmalogen-containing food on cognitive function in patients with mild Alzheimer's disease or mild cognitive impairment - a double blind trial - (Registration No. UMIN000014945) Administration period: 7 months, Participating facilities: 25. Study was completed in April, 2016.

■ Open label study (number of confirmed subjects: 225)

Study title: Effect of plasmalogen-containing food on cognitive function in patients with dementia (except mild Alzheimer's disease) - an open trial - (Registration No. UMIN000016008) Study period: 3 months, Participating facilities: 26, Subjects: Patients with all types of dementia including, moderate and severe disease and dementia with Lewy Bodies. Study was completed in April, 2016

The following members of the Japanese Plasmalogen Society have been at the core of fundamental and medical research on plasmalogen.

The Japanese Plasmalogen Society

6F, 6-18 Tenyamachi, Hakata-ku, Fukuoka-shi, Fukuoka, 812-0025
The Japanese Plasmalogen Society HP: www.pls.jp

This society aims to contribute to the treatment and prevention of disorders such as Alzheimer's disease, depression, Parkinson's disease, behavioral disorders such as truancy, and metabolic syndrome, as well as conducting academic activities to share the product of their achievements with society, through joint research on plasmalogen, and in turn, research on "brain fatigue". The following projects are being conducted in order to achieve this goal.

① Joint research and contract research towards this purpose.
② Publication of results at research meetings and lectures which are held at least once a year.
③ Other projects necessary to achieve the goals of the society

Members

President	Yutaka Omura (Emeritus Professor/ Department of Integrative Physiology, Kyushu University Graduate School of Medicine)
Vice President	Takehiko Fujino (Emeritus Professor/ Institute of Health Sciences, Kyushu University School of Medicine)
〃	Yukio Fujiki (Professor/ Department of Biology, Faculty of Science, Kyushu University Graduate School of Science)
〃	Toshihiko Katafuchi (Associate Professor/ Department of Integrative Physiology, Kyushu University Graduate School of Medical Sciences)
Directors	Shiro Mawatari (Director/ Institute of Rheological Functions of Food/Department of Neurology, Neurological Institute, Kyushu University Graduate School of Medical Sciences)
〃	Yoshio Tsuboi (Professor/ Department of Neurology, Fukuoka University School of Medicine)
〃	Tatsuo Yamada (Kyojunokai)
〃	Takashi Asada (Professor/ Graduate School of Comprehensive Human Sciences Majors of Medical Sciences, University of Tsukuba)
〃	Junichi Kira (Professor/Department of Neurology, Neurological Institute, Kyushu University Graduate school of Medical Sciences)
Auditor	Shinji Oma (Associate Professor/ Department of Neurology, Fukuoka University School of Medicine)
Adviser	Nobuyuki Nakahara (Chairman/ The American Studies Foundation/ Formerly Council member/ Policy board of the Bank of Japan)
Advisor on clinical trial statistics	Suminori Kono (Chairman/ National Institute of Health and Nutrition)
Members	Masanori Honjo (Assistant Professor/ Kyushu University School of Science), Tsutomu Hoshuyama (Lecturer/ University of Occupational and Environmental Health), Tatsuo Okauchi (Associate Professor/ Kyushu Institute of Technology), Mitsuru Kitamura (Associate Professor/ Kyushu Institute of Technology)

Published papers relating to plasmalogen

Paper 1: Separation of plasmalogen in cell membranes using HPLC method

Separation of intact plasmalogens and all other phospholipids by a single run of high-performance liquid chromatography.Analytical Biochemistry 370(2007)54-59

Paper 2: Anti-neuroinflammatory/anti-amyloidogenic effects

Anti-inflammatory/anti-amyloidogenic effects of plasmalogens in lipopolysaccharide-induced neuroinflammation in adult mice. Journal of Neuroinflammation 2012, 9:197

Paper 3: Increase in blood plasmalogen through oral administration

Dietary plasmalogen increases erythrocyte membrane plasmaogen in rats.Lipids in Health and Disease 2012,11:161

Paper 4: Changes in phospholid composition in Alzheimers disease

Changes in Phospholid Composition of Erythrocyte Membrance in Alzheimers Disease.Dement Geriatr Cogn Disord Extra 2012(2),298-303

Paper 5: Anti-apoptotic effect of plasmalogen

Plasmalogens rescue neuronal cell death through an activation of AKT and ERK survival signaling. PLos ONE 2013, 8: e83508

Paper 6: Activation of plasmalogen protein kinase by orphan G-protein coupled receptor

Neuronal orphan G-protein coupled receptor proteins mediate plasmalogens-induced activation of ERK and Akt signaling. PLos ONE. 2016, 11: e0150846

◆Information on explanatory videos and books about Plasmalogen

The cause of dementia is "brain fatigue"!? Plasmalogen is shown to improve dementia. Finally in book form, the particulars and evidence.

解説動画配信 (解説動画 YouTube 画面)

バーコードリーダーアプリで読み込み、ご覧ください。