

**Case Presentation**

**Submission Date: September 11, 2023**

**Acceptance Date: February 22, 2024**

**Publication Date: March 01, 2024**

**Ginkgo Biloba Extract Containing Plasmalogen May Improve  
Brain Function Decline Including Brain Fog**

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## **Abstract**

Deterioration of brain function, including brain fog, is currently becoming a serious problem as it impairs daily life and quality of life. When it comes to decline in brain function, degenerative diseases such as Alzheimer's disease are often cited, but in reality, it is also thought to be caused by a decline in cerebral blood flow and a decline in neurotransmitters in the brain. Therefore, this time, we will report on a case report as we administered plasmalogen-containing ginkgo biloba extract to people who complain of decreased brain function, including brain fog, in cases other than degenerative diseases such as Alzheimer's dementia, and found that it had a certain effect. I would like to report as.

**Keywords:** Brain fog; Ginkgo biloba extract; Plasmalogen, Cerebral blood flow; Cognitive function

## **Introduction**

Currently, it has been reported that brain function has decreased due to stress due to social situations and infection with COVID-19 [1,2]. Declining brain function not only reduces QOL but also seriously impedes ADL, so countermeasures are urgently needed. Although it is not a specific disease name, brain fog, which is a state in which the brain is foggy, is a serious social problem [3]. Brain fog deteriorates cognitive function [4] and is manifested by persistent fatigue, malaise, decreased cognitive function, and difficulty returning to work, and perceived stress [5]. Although the mechanism is still largely unknown, it is hypothesized that it may be caused by a decrease in cerebral blood flow [6] or impaired neurotransmitter transmission [7]. In particular, after being infected with COVID-19, brain fog is often seen as an aftereffect, so it was once a problem [8]. According to the World Health Organization (WHO), "symptoms that occur in people with COVID-19, persist for at least two months, and are unexplained as symptoms of another disease (usually within three months of the onset of COVID-19)" [9] defines sequelae (post-COVID-19 condition). In particular, in the case of post-COVID-19 conditions (aftereffects), there is concern that the secretion, action, and release of the neurotransmitter acetylcholine

may be insufficient [10], resulting in a brain fog-like state that continues. It is characterized by central nervous system symptoms such as [11], loss of concentration [12], feeling tired all the time [13], and being unable to understand the content even though the voice is heard even when spoken to [13].

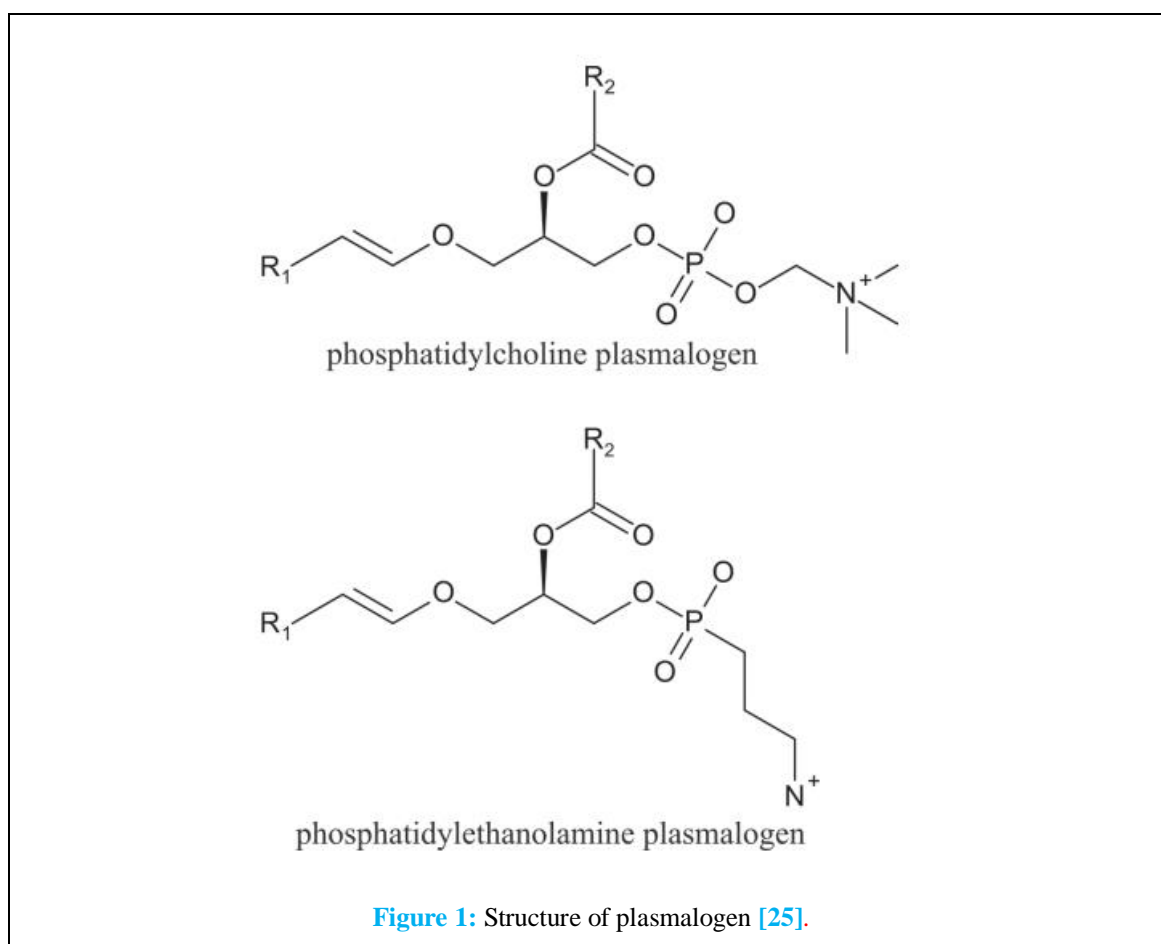
This is sometimes diagnosed as depression, and it is said that depression is caused by insufficient secretion of serotonin [14], but brain fog is partly related to serotonin as a neurotransmitter. Although the possibility cannot be denied, the main neurotransmitter is acetylcholine, so even if anti-anxiety drugs or anti-depressants are prescribed, there is a high possibility that they will not be effective. Furthermore, if anxiolytics or antidepressants are administered, although they are not currently recommended, long-term administration may lead to problems such as dependence [15]. Therefore, it is extremely difficult to differentiate between the two, and there is a need to establish clear diagnostic criteria for depression and brain fog in the future. However, since there is an urgent need to approach brain fog at this stage, the purpose of this study was to use functional foods to examine the effects of improving brain fog, including the decline in brain function. Although this is still a hypothesis, in patients with decreased brain function, there are two possible causes: lack of stimulation to the brain and decreased blood flow to the brain, so it may be possible to improve these functions by approaching them at the same time. It was thought. Therefore, the substance we used this time is a mixture of plasmalogen [16], which is said to be good for cognitive function, and ginkgo biloba extract [17], which is said to improve blood flow. We obtained good results and would like to report them here.

## **Materials**

### **Plasmalogen**

Plasmalogen is one of the components of the myelin sheath in the nervous system [18]. In addition, it is present in large numbers in the immune system and circulatory system [19]. In human heart tissue, approximately 30-40% of choline glycerophospholipids are said to be plasmalogens [20]. It is also said

that approximately 30% of the glycerophospholipids in the adult brain and up to 70% of the ethanolamine glycerophospholipids in the myelin sheath are plasmalogens, so it can be said that they are closely related to cognitive function [21]. Plasmalogens are also said to have antioxidant effects, and it has been suggested that they protect the brain from reactive oxygen species while repairing myelin sheaths [22]. Active oxygen species are thought to cause various diseases [23]. Plasmalogen was selected because it has been suggested that reactive oxygen species are involved in the decline in brain function [24] (Figure 1).



### Ginkgo biloba

Ginkgo biloba leaves contain ginkgolide, a type of terpenoid [26]. Ginkgolide has the ability to inhibit

platelet activating factors and is used as a substance that improves blood flow [27]. In this study, ginkgo biloba was used for the purpose of improving cerebral blood flow. It is also said that ginkgo biloba leaves have the effect of removing reactive oxygen species [28], and in addition to plasmalogen, using ginkgo biloba leaves can be expected to have further antioxidant effects (Figure 2).

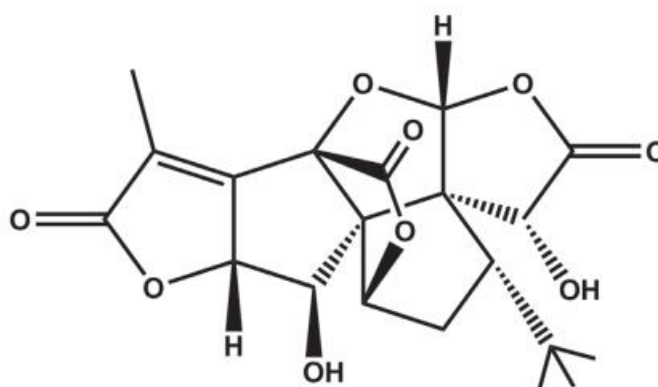


Figure 2: Structure of ginkgolide [29].

### Case Presentation

With the approval of the Hino Kosei Clinic Ethics Committee (HKC\_N20022023), participants ingested a mixture (Dialethea<sup>®</sup>) of 1 mg of plasmalogen and 140 mg of ginkgo biloba extract per day for 14 days, and then completed an anonymous online questionnaire. I did a tally (n=37). Since this study is an approach to the decline in brain function, the subjects were not only patients diagnosed with brain fog, but also ordinary people who had recently noticed symptoms of a decline in brain function. In addition, patients who were taking daily medications such as antidepressants and anti-anxiety drugs were included as exclusion criteria.

The questionnaire items were created based on the content carefully reviewed by the Brain Fog Study Group.

| Question  | Answer                                       |
|---|--|
| 1. Sex  | Men: 45.9%<br>Women:<br>54.1%                |
| 2. Have you noticed any changes in your physical condition after taking ginkgo biloba extract containing plasmalogen? | Yes: 86.5%<br>Not sure:<br>13.5%<br>None: 0% |
| 3. Questions for people with changes in physical condition  |  |
| 1) mentally   |  |
| I felt like my head was clearer   | 59.4%  |
| Improved forgetfulness and memory   | 21.9%  |
| concentration improved  | 37.5%  |
| My energy has improved  | 43.8%  |
| Irritability has improved   | 21.9%  |
| Reduced brain fatigue   | 31.3%  |
| Reduced fatigue and stress  | 25%  |
| Work that uses your head has become easier  | 34.4%  |
| 2) Physical condition   |  |
| sleep improved  | 37.9%  |
| My headache has improved  | 37.9%  |
| I got rid of my fatigue.  | 27.6%  |
| going out more  | 10.3%  |
| 3) Free description   |  |

|                        |       |
|------------------------|-------|
| improved concentration | 59.4% |
| enthusiasm for things  | 50%   |
| Improvement of fatigue | 46.9% |

As mentioned above, men and women and age groups responded equally to the questionnaire, confirming that this symptom can occur in anyone, regardless of gender or age differences. In addition, the percentage of questions regarding improvement in brain function, including brain fog, was significantly high. (Chi-square test,  $P < 0.05$ ).

## Results

Looking at the questionnaire, it was found that people who took ginkgo biloba extract containing plasmalogen for 14 days experienced positive changes in their physical condition. 0 answered that there had been no particular change, 86.5% said there had been a change, and 13.5% said they were not sure, but there might have been some change. From these cases, cases in which the physical condition changed positively were extracted, and the changes that occurred are shown in the table below. Looking at the overall numbers, it can be seen that there has been a significant improvement. (Chi-square test,  $P < 0.05$ ).

## Discussion

In this study, we approached the decline in brain function, including brain fog, and confirmed cases of improvement. Although it is still unknown as I am still taking it, I can expect to see a number of improvements. As the name suggests, plasmalogen-containing ginkgo biloba extract is a mixture of plasmalogen and ginkgo biloba extract. Plasmalogens are generally said to help improve cognitive function [30,31]. This time, we set a daily intake of 1000 µg of plasmalogen extracted from chicken breast. In addition, ginkgo biloba extract [32], which is said to be related to the removal of active oxygen and improvement of blood flow, is also added, and it can be said that this is a substance that

simultaneously approaches the improvement of cerebral blood flow and cognitive function. Decline in brain function has a strong impact on daily life. As the name suggests, brain fog is a state in which your brain continues to be foggy [33], you lose the ability to concentrate [34], you feel tired all the time [35], and even though you hear voices even when you talk to them, a decline in cognitive function that causes an inability to understand the content. These are not medically defined diseases, but are defined only as symptoms [1]. In addition, Alzheimer's type dementia and Lewy body dementia can be cited as causes of decline in brain function, but these are caused by proteins called  $\beta$ -amyloid and Lewy bodies [33], which accumulate in the brain., it is known that it inhibits neurotransmitters in the brain [34], resulting in a significant decline in brain function. Putting these theories together, it is highly possible that the decline in cognitive function, including brain fog, is caused by the suppression of neurotransmitter release [12]. Therefore, in the research conducted this time, by improving cognitive function with the aforementioned plasmalogen and improving cerebral blood flow with ginkgo biloba extract, we were able to improve the blood flow of blood vessels to the brain derived from the circle of Willis. It is thought that sufficient oxygen can be delivered. Furthermore, by improving the myelin sheath with plasmalogen, it is possible to appropriately release neurotransmitters, and it is fully suggested that brain function may be improved as a result. In the future, it will be necessary to prove how plasmalogen-containing ginkgo biloba extract acts on the brain. At the same time, there is a good possibility that we can study the functionality of diseases related to blood flow, so we would like to study cardiovascular diseases as well.

### **Acknowledgment**

We would like to express our deep gratitude to the directors of the Japan Society of Preemptive and Clinical Medicine “JSPCM” for their cooperation in creating the questionnaire items for this study.

### **Ethical Considerations**



This study was conducted after obtaining approval from the Hinokosei Clinic Ethics Committee. (HKC\_N20022023).

### **Conflict of Interest**

There are no conflicts of interest in this research.

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### **Citation of this Article**

Kawakami S, Tanaka Y, Usui M, Iida S, Shirakawa T and Fukuzawa Y. Ginkgo Biloba Extract Containing Plasmalogen May Improve Brain Function Decline Including Brain Fog. *Mega J Case Rep.* 2024;7(2):2001-2012.

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