

## Transported amount of diosgenin to the brain is differed by a solvent fat

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### Abstract

We previously reported effects of diosgenin on cognitive function in normal mice and Alzheimer's disease model mice and healthy humans. The low oral bioavailability of diosgenin has been well recognized. However, our previous study showed that diosgenin dissolved in olive oil was efficiently distributed in the brain and exerted a memory-enhancing effect in mice after oral administration. This study investigated potencies of olive oil, fish oil and medium-chain triglyceride to transfer diosgenin in the brain. Diosgenin detected in the cerebral cortex after oral administration was very high in case of dissolved in olive oil. Brain penetration of diosgenin dissolved in fish oil was lower than that in olive oil. Medium-chain triglyceride showed very low potential of brain penetration of diosgenin after p.o. administration. We found in this study potencies of transporting diosgenin to the brain were different by fats as solvents.

**Keywords** : diosgenin, brain transfer, olive oil, fish oil, medium-chain triglyceride

## I Introduction

We reported effects of diosgenin on cognitive function in normal mice<sup>1, 2)</sup> and Alzheimer's disease model mice<sup>3, 4)</sup> and healthy humans<sup>2)</sup>. The low oral bioavailability of diosgenin has been well recognized. This low absorption has been attributed to the poor solubility of diosgenin in water, and a previous rat study therefore proposed the formation of a complex with cyclodextrin to increase solubility<sup>5)</sup>. However, our previous study showed diosgenin had no effect on memory function in mice, despite successful solubilization when diosgenin was dissolved in a 10% ethanol-5% glucose solution<sup>2)</sup>. In contrast, diosgenin dissolved in olive oil was efficiently distributed in the brain and exerted a memory-enhancing effect in mice<sup>2)</sup>. We previously got evidences showing same potencies of olive oil, sesame oil and soybean oil for diosgenin transfer in the brain. However, it has not been compared that other kinds of fats have an ability of diosgenin transfer in the brain. Therefore, this study investigated potencies of olive oil, fish oil and medium-chain triglyceride (caprylic/capric triglyceride) to transfer diosgenin in the brain.

## II Materials and Methods

### 1. Animal studies

All experiments were performed in accordance with the Guidelines for the Care and Use of Laboratory Animals of the University of Toyama. The Committee for Animal Care and Use at the Sugitani Campus of the University of Toyama approved the study protocol (approval number for the animal experiments is A2017INM-1). All efforts were made to minimize the number of animals used.

Male ddY mice (8 weeks old, male) were purchased from Japan SLC (Shizuoka, Japan). All mice were housed in a controlled environment (25 ± 2°C, 12 h light/dark cycle starting at 7:00 am) with free access to food and water. Sixteen hours before administration of the sample, fasting was started.

### 2. Drug administration

Diosgenin compound was purchased from LKT Laboratories (St. Paul, Minnesota, USA). We dissolved 8 mg diosgenin in 790 µl of each oil using a micromixer. Oils used in this study