

# 学位論文の要旨

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学位論文名 Oral Intake of Encapsulated Dried Ginger Root Powder Hardly Affects Human Thermoregulatory Function, but Appears to Facilitate Fat Utilization

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## 論文内容の要旨

### INTRODUCTION

The components of root of Ginger (*Zingiber officinale* Roscoe, Zingiberaceae) have been widely used for various medicinal purposes in Asia for thousands of years. A variety of active components of ginger have been identified. Among them, 6-, 8-, and 10-gingerols and 6-shogaol have been intensively investigated as remedies for medical use. In Japan, one of the generally acknowledged beneficial effects of ginger consumption is an induction of a “warm sensation”, although the meaning of the phrase is vague. In rats, an intraperitoneal injection of 6-gingerol lowered core body temperature ( $T_{cor}$ ) by depressing metabolic heat production, suggesting that ginger components modify thermoregulatory function in animals. Thus, the primary purpose of the present study was to investigate the impact of the intake of a practical dose of ginger root extract on heat balance,  $T_{cor}$  and blood energy substrate levels comprehensively in humans.

Recently, oral intake of ginger components for several weeks has been shown to modify fat metabolism in rodents with alcohol-induced fatty liver. In addition, long-term administration of ginger components appears to enhance fat utilization in animals and humans. However, there are no data on how a single dose of ginger affects fat oxidation in humans. Free fatty acids (FFA) derived from triglycerides (TG) are known to be essential energy substrates, especially in nonshivering thermogenesis. We, therefore, investigated the effects of single ingestion of ginger powder on serum FFA levels and fat oxidation.

### MATERIALS AND METHODS

This study was approved by the Ethical Committee for Human Experimentation of the School of Medicine, Shimane University, Japan. Ginger and placebo capsules, each containing 250 mg of dried ginger root powder or of starch, were manufactured. In all experiments, each subject ingested 1.0 g of dried ginger root powder or starch. The capsules were ingested with 200 ml of temperature-controlled warm water (37°C) to avoid thermal stimulation to the subjects.

Experiment 1: effects of ginger intake on thermal balance,  $T_{\text{cor}}$  and blood energy substrates levels

Healthy male subjects entered a temperature-controlled room with an ambient temperature ( $T_a$ ) of 28.0°C and relative humidity of 50% in the morning ( $n = 5$ ) or afternoon ( $n = 4$ ). After 30-min rest, the subjects ingested ginger capsules or a placebo. Rectal temperature ( $T_{\text{re}}$ ), skin temperatures, sweating rates ( $\dot{m}_{\text{sw}}$ ), skin blood flows (skBF),  $\text{O}_2$  consumption ( $\dot{V}_{\text{O}_2}$ ), and  $\text{CO}_2$  production ( $\dot{V}_{\text{CO}_2}$ ), and heart rate (HR) were measured between 30 min before and 120 min after capsule intake. The subjects voted scales of whole body thermal sensation and thermal comfort every 30 min. Blood sample was taken 30 min before and 120 min after capsule intake.

Experiment 2: effects of ginger intake on threshold  $T_{\text{cor}}$  for skBF and  $\dot{m}_{\text{sw}}$

Four healthy male subjects were exposed to the same environments as in Experiment 1 in the afternoon. At 30 min after ginger or placebo intake, the subjects immersed both legs in a water-bath in which the water temperature was controlled at 42.0°C. The warm water immersion continued for 30 min. Skin temperatures,  $T_{\text{re}}$ , skBF, and  $\dot{m}_{\text{sw}}$  were continuously measured.

Experiment 3: effects of ginger intake on serum FFA profile

Five healthy male subjects entered a room with a  $T_a$  of 25.0°C in the afternoon. After 30 min, the subjects ingested either ginger capsules or a placebo. Just prior to ginger or placebo capsule intake (0 min), and at 30, 60, and 120 min after ginger or placebo intake, a blood sample was taken. Serum was separated from the blood immediately and kept at -80°C until analyses. The serum FFA profiles were determined by gas chromatography. FFAs were classified according to carbon number, long chain fatty acids (LCFA, carbon chain 16-18) and very long chain fatty acids (VLCFA, carbon chain > 20).

## **RESULTS AND DISCUSSION**

Experiment 1: effects of ginger intake on thermal balance,  $T_{\text{cor}}$  and blood energy substrates levels

In both morning and afternoon tests, there were no significant differences between the ginger and placebo ingestion groups in changes of  $T_{\text{re}}$ ,  $T_{\text{sk}}$ , finger and forearm skBFs, palm and forearm  $\dot{m}_{\text{sw}}$ ,  $\dot{V}_{\text{O}_2}$  and  $\dot{V}_{\text{CO}_2}$ . Furthermore, ginger intake did not affect the scores of whole body thermal sensation and thermal comfort. The results suggest that a single oral ginger administration hardly affects  $T_{\text{cor}}$ , thermal balance, and behavioral thermoregulation in humans. In rat study, 6-gingerol was directly injected into the intraperitoneal cavity and induced a fall in  $T_{\text{cor}}$ . Thus, plasma levels of the free active ginger component in rats were thought to be much higher than that in the present human subjects, which may have then induced the discrepancy of the effects of ginger components on thermoregulatory system between humans and rats.

In respiratory exchange ratio (R) calculated as  $\dot{V}_{CO_2} / \dot{V}_{O_2}$ , there were significant differences in the time course ( $F_{4,16} = 4.332$ ,  $P = 0.015$ ) and interaction between ginger intake and time ( $F_{4,16} = 3.432$ ,  $P = 0.033$ ) only in the morning. R values at 60 ( $P = 0.043$ ), 90 ( $P = 0.008$ ) and 120 ( $P = 0.001$ ) min after ginger ingestion were significantly lower than that just before ginger intake. Then, the rates of fat oxidation were calculated using stoichiometric equations. Fat oxidation was significantly elevated by 13.5% at 120 min after ginger ingestion, while it decreased by 2.2% after placebo intake. Thus, a single oral ginger ingestion seemed to increase fat oxidation in humans, although timing may be of relevance.

Serum FFA levels after ginger ingestion were significantly greater than that before ingestion ( $P = 0.005$ ) in the morning. Placebo ingestion also significantly elevated serum FFA levels ( $P = 0.043$ ). In the afternoon, ginger ingestion significantly elevated serum FFA levels ( $P = 0.040$ ), while placebo intake had no significant affect ( $P = 0.125$ ). The results suggested that a single oral ingestion of ginger powder plays a significant role in an increase in serum FFA levels in humans.

Experiment 2: effects of ginger intake on threshold  $T_{cor}$  for skBF and  $\dot{m}_{sw}$

The onsets of skin vasodilation and thermal sweating were identified by the prompt increases of skBF and  $\dot{m}_{sw}$ , respectively, and threshold mean body temperatures and latencies for nonevaporative and evaporative heat losses were determined. However, ginger ingestion did not alter the thresholds and latencies, suggesting that oral ginger intake has no significant effects on thermoregulatory centers in humans.

Experiment 3: effects of ginger intake on serum FFA profile

There were significant effects of ginger intake ( $F_{1,4} = 51.880$ ,  $P = 0.002$ ) and time ( $F_{3,12} = 6.941$ ,  $P = 0.006$ ) on the mol% of LCFAs (for interaction, ( $F_{3,12} = 14.974$ ,  $P < 0.001$ )). In addition, the mol% of LCFAs after ginger ingestion was significantly lower than that after placebo ingestion at 30 ( $P = 0.006$ ), 60 ( $P = 0.045$ ) and 120 min ( $P = 0.006$ ) after oral intakes. Similarly, ginger ingestion and time had significant influence on the mol% of VLCFAs. The mol% of VLCFAs was significantly greater in subjects treated with ginger than that in subjects administered with placebo at 30, 60 and 120 min after oral ingestion (statistical values are the same as in the mol% of LCFAs). The finding suggests that the increased serum FFA levels due to oral ginger ingestion seemed to be attributable to the rises in VLCFAs.

## CONCLUSIONS

In human subjects, the effects of a single oral intake of 1.0 g of dried ginger powder on the peripheral and central thermoregulatory function is miniscule. However, ginger administration elevates serum FFA levels and may facilitate fat utilization, though timing may have some relevance.