（学位第３号様式）

学 位 論 文 要 旨

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題　目	Studies on the safety and functionality of bioactive substances derived from Wasabi (*Eutrema japonicum* (Miq.) Koidz.) （わさび由来生理活性物質の安全性と機能性に関する研究）

Wasabi, a plant native to Japan, is known to have been used as a medicinal herb from ancient times to modern times. It is used as a basic condiment in Japanese cuisine. Its root parts and stems are used as a condiment, but most of its leaves are discarded. In addition, the number of farmers engaging for cultivating wasabi, and the amount of wasabi consumed in Japan are decreasing. In order to create new value for revitalizing the wasabi industry and utilization, in present study, I conducted to investigate the safety and functionality of wasabi.

First, the safety evaluation of the wasabi leaf (WL) was conducted with the assays of the mutagenicity, acute and sub-acute toxicity, and human safety trial. The results from toxicity test showed that WL extracts (WLE) did not show mutagenicity up to 5000 μg/plate. WLE were not observed that acute toxicity in mice administered 5000 mg/kg/day and sub-acute toxicity in rats administered 2500 mg/kg/day. Twelve healthy subjects, aged 20–64 years and mildly obese (BMI 23.0 to 30.0 kg/m^2), were enrolled in the clinical trial, and ingested 200 mg/day WLE for 12 weeks. Ingestion of 200 mg/day of WLE was demonstrated to be safe. These data provide the first standard references for wasabi leaf supplement application. Additionally, ingestion of 200 mg/day of WLE powder had effects in the reduction of visceral fat although the number of subjects in the present clinical trial was small.

Next, 6-(Methylsulfinyl) hexyl isothiocyanate (6-MSITC) has recently been reported to have antioxidant and brain function improvement effects, and its use is expected to expand in the future. However, its safety has not been reported. The safety evaluation of 6-MSITC and Wasabi sulfinyl (WS), a wasabi rhizome extract powder containing 0.8% 6-MSITC, was conducted by a toxicity test and human clinical trial. Our data showed that no mutagenicity was observed and Lethal dose 50 values of synthetic 6-MSITC were estimated to be 451.2 mg/kg in male rats and 400.7 mg/kg in female rats. No sub-acute toxicity was observed in rats administrated WS at 2,500 mg/kg/day. In human trial, ingestion of 500 mg/day of WS was demonstrated to be safe at the least. Our data on the safety evaluation of 6-MSITC and WS provide the first standard references for wasabi rhizome supplement application.

Finally, WL and isosaponarin, a flavonoid contained in the WL, was found to enhance the proliferation of human follicle dermal papilla cells (DPCs) in culture cells. Moreover, isosaponarin increased the amount and activities of mitochondrial and the productions of vascular endothelial growth factor (VEGF). Furthermore, the data from human clinical trials by applying isosaponarin-rich WL to 21 subjects who has scalp essence for 8 weeks showed that hair loss was reduced about 60% and scalp redness and itching were also suppressed.

These results indicate that the roots and leaves of wasabi are safely used in the general range of now consumption and have various functional properties. Moreover, these data will provide standard references for safe utilization of wasabi rhizome and leaves, and will help to revitalize wasabi industry.