（学位第３号様式）

学 位 論 文 要 旨

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題　目	Studies on preventive effects and mechanisms of garlic on dyslipidemia and gut microbiota dysbiosis（ニンニクによる脂質異常症及び腸内細菌叢失調の予防効果及び作用機構に関する研究）

Garlic (*Allium sativum*) as a favorite health food has many functions. Especially, it has been reported that organosulfur compounds (OSCs) in garlic have the potential to improve lipid and glucose metabolism and regulate lifestyle-related diseases. However, the metabolic mechanisms on its function, and whether this function is related to gut microbiota remain unclear. In this study, the modes of animal experiment and bacterial culture in dyslipidemia and gut microbiota dysbiosis were used to investigate the effect and mechanism of garlic OSCs on gut microbiota, lipid and glucose metabolisms.

Firstly, the mice were fed with the high-fat diet (HFD) to induce dyslipidemia and gut microbiota dysbiosis, and HFD supplemented with 5% garlic for 12 weeks to investigate the effect. The result revealed that garlic supplementation attenuated HFD-enhanced ratio of serum GPT/GOT, the levels of total cholesterol and low-density lipoproteins. In addition, garlic supplementation was increased the relative abundance of f_*Lachnospiraceae*, while reduced the relative abundance of g_*Prevotella*. Therefore, garlic supplementation could meliorate the HFD-induced dyslipidemia and gut microbiota dysbiosis.

Secondly, we obtained alliinase-free garlic (AFG) with stable OSCs by inactivating the garlic alliinase. The effect of AFG on dyslipidemia and gut microbiota dysbiosis were further investigated. The results revealed that AFG supplementation attenuated HFD-enhanced ratio of serum GPT/GOT. The ratio of p-*Firmicutes* to p-*Bacteroidetes* increased by aging and HFD was reduced by AFG. The AFG enhanced the f-*Lachnospiraceae*, g-*Akkermansia*, and g-*Lactobacillus* which were decreased by aging and HFD. AFG meliorated HFD-induced dyslipidemia and improve individual characteristic gut bacteria.

Thirdly, in order to clarify the effect and mechanism of AFG on the lipid and glucose metabolism, we used western diet (WD) containing high fat, high cholesterol and sugar. AFG with different OSCs concentrations was added to WD, with which the mice were fed for 12 weeks. Results revealed that garlic OSCs caused an increase in gut taurine and an inhibition of DPP-4, and ameliorated WD-induced disorders of lipid and glucose metabolism. Especially, the gut commensal *Bacteroides acidifaciens* (*B. acidifaciens*) was significantly increased by garlic OSCs. In *in vitro* culture, OSCs markedly increased the growth of *B. acidifaciens* growth in a dose-dependent manner. These data demonstrated that *B. acidifaciens*-taurine axis / DPP-4 axis was involved in the preventive effect of garlic OSCs on WD-induced metabolic disorder of lipid and glucose.

In conclusion, garlic OSCs has the preventive effects on metabolic syndrome and gut microbiota disorder induced by over nutrition diet. Moreover, stable components and effects of garlic OSCs could be obtained by inactivating garlic alliinase. Furthermore, the mechanism of garlic OSCs on the regulation of lipid and glucose metabolism were clarified that OSCs enhanced the proliferation of the *B. acidifaciens* to produce taurine and inhibit DPP-4. These results will provide new insight for understanding the molecular mechanisms of garlic on the prevention of lifestyle-related diseases and gut microbiota disorder, and the scientific basis for the application of garlic in functional food.