Studies on anti-obesity compounds in Okinawan traditional bioresources: Identification and its activity enhancement.

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Abstract

Supplementation of diet with functional components is an effective way to manage obesity and overweight. Therefore, this study aims to characterize the anti-obesity properties of Okinawan folk medicine and attempt the enhancement of their bioactivities.

The first experiment examined the anti-obesity mechanisms of dihydropyranocoumarins (DPCs). In the previous studies, DPCs were isolated from an Okinawan traditional herb, *Peucedanum japonicum* Thunb. (PJT), as anti-obesity compounds with cultured adipocytes. However, it is not known whether DPCs exert anti-obesity activity *in vivo*. I also assessed the effect of nanoparticulation of DPCs into polylactic-co-glycolic acid (PLGA) on their bioavailability and functionality. Dietary intake of DPCs significantly suppressed the body weight gain and fat accumulation in white adipose tissues (WAT) of mice fed a high-fat diet. DPCs intake also significantly decreased the mean size of adipocytes and upregulated mRNA levels of thermogenesis-related genes in WAT. Similar results were observed in mice received a small amount of DPCs (1% equivalence of regular dose) when encapsulating in PLGA nanoparticles, but not non-nanoparticulated form. These results suggested that DPCs' anti-obesity properties are caused by an increase in energy expenditures, and that a PLGA-based nanoparticulate system is a powerful tool to enhance their activities.

Next, I focused on anti-obesity properties of *Cirsium brevicaule* A. GRAY (CBAG), whose aerial parts and root are traditionally used as both food and herbal medicine in Okinawa. Our previous study demonstrated the anti-obesity properties of CBAG leaves, but not evaluated the biological activities of CBAG root (CbR). This study therefore evaluated and characterized the anti-obesity properties of CbR by testing its activities in adipocyte cultures. Dried CbR powder was serially extracted with solvents of various polarities, and these crude extracts were tested for inhibitory effects on lipid accumulation in 3T3–L1 cells. Treatment of 3T3–L1 cells with a methanol extract of CbR reduced cellular lipid accumulation the most. The methanol extract was then fractionated, and these fractions were subjected to further activity analyses. The phenylpropanoid glycosidic molecule syringin (PubChem ID: 5316860) was identified as an active compound in CbR. Syringin suppressed lipid accumulation of 3T3–L1 cells in a dose-dependent manner without cytotoxicity. This compound also significantly reduced the gene expressions of the master regulator of adipogenesis and other differentiation markers, and effectively enhanced the phosphorylation of the AMP-activated protein kinase and acetyl-CoA carboxylase. These results indicated that syringin has potent anti-obesity effects due to the attenuation of adipocyte differentiation, adipogenesis, and the promotion of lipid metabolism.

In conclusion, the results of present studies provide insight into the anti-obesity characteristics of DPCs and syringin, suggesting the great potential of PJT and CBAG as functional foods against obesity. In addition, this study pointed to the great potential for a PLGA-based nanoparticle encapsulation of bioactive compounds such as DPC in the oral delivery of anti-obesity agents.