Abstract

Background

Glucoraphanin (GR) is a natural glucosinolate abundantly found in broccoli sprouts. GR is converted to sulforaphane by myrosinase enzyme and the metabolite is a potent activator of a nuclear factor (erythroid-derived 2)-like 2 (Nrf2). Activation of Nrf2 induces antioxidant and detoxication-related genes, thus leading to cellular protection against oxidative stress. We have demonstrated that GR has preventive effects on impairment of glucose homeostasis in diet-induced obese (DIO) mice via an increment in energy expenditure, shifting macrophage polarization in liver and adipose tissue, and changing microbiota characteristics.

Aim

Herein, we aimed to elucidate the therapeutic effects of GR on obesity and hepatic steatosis using a murine model.

Method

Five-week-old male C57BL/6J mice were fed a high-fat diet (HFD) for

9 weeks, and then these DIO mice were maintained on a normal chow diet (NC) or HFD with or without 2.2% GR (HFD, HFD-GR, NC, and NC-GR) for further 11 weeks.

1. **Results**

GR significantly suppressed a transient weight gain ($p < 0.01$) in the group fed either with a NC or HFD. However, there was no significant difference on body weight at a termination of this study (25 weeks of age) in both of a NC and HFD groups. GR improved hepatic steatosis. Plasma enzyme activity levels of alanine transaminase (ALT) and aspartate transaminase (AST) were significantly lowered in a HFD-GR group than that in a HFD group ($p < 0.05$). Histological analysis and biochemical assays showed a decrease in the accumulation of lipid in liver of a HFD-GR group. These results were accompanied by the increased expression of β-oxidation genes (Ppar α and Cpt1 α)($p < 0.05$) and the decreased expression of lipogenic genes (Srebp-1c , Acc and Scd1) ($p < 0.05$). GR also improved hepatic inflammation in HFD-fed mice. GR

suppressed inflammatory signaling including c-Jun N-terminal kinase (JNK) ($p < 0.05$). Moreover, a flow cytometry analysis revealed that GR did not affect the number of liver macrophages identified as $CD45^{+}CD11b^{+}F4/80^{+}$ cells in mice fed either a NC or HFD, however HFD-GR mice had 12% fewer $CD11c^{+}CD206^{-}$ (M1) macrophages but 230% more $CD11c^{-}CD206^{+}$ (M2) macrophages in liver, resulting in a predominance of the M2 compared to the M1 macrophage population in liver. Thus, these findings suggest that glucoraphanin has the therapeutic effects on hepatic inflammation and steatosis through shifting macrophage polarization in male DIO mice.

Discussion

Thus, these findings suggest that glucoraphanin has the therapeutic effects on hepatic inflammation and steatosis through shifting macrophage polarization in male DIO mice.

References

1. Nagata N, et al. Glucoraphanin Ameliorates Obesity and Insulin Resistance Through Adipose Tissue Browning and Reduction of Metabolic Endotoxemia in Mice. Diabetes. 2017;66(5):1222-1236.