Comparison of enzymatically synthesized inulin, clofibrate and fluvastatin effects on biomarkers of metabolic disease and drug metabolism in rats fed standard and cafeteria diets

Junko Sugatani, Makoto Osabe, Satoshi Sadamitsu, Masaki Imanishi, Yasuhiro Yamazaki, Akira Ikari and Masao Miwa

Global COE Program, Department of Pharmaco-Biochemistry, Graduate School of Pharmaceutical Sciences, University of Shizuoka

Inulin enzymatically synthesized from sucrose is a dietary component that completely escapes glucide digestion. Our study aimed at distinguishing health effects of synthetic inulin with different degrees of fructose polymerization (DP) from those of resistant maltodextrin, clofibrate, and fluvastatin. Supplementing inulin to a high-fat and high-sucrose (HF, cafeteria) diet ameliorated hypertriglycemia and hepatic steatosis in 3-week-fed rats. Inulin (average DP=16~17) significantly reduced the portal plasma glucose level. The levels of portal plasma propionate and circulating serum adiponectin, which were decreased in cafeteria rats, recovered to nearly normal levels after administration of inulin (average DP=16~17). In addition, the dietary inulin suppressed elevation in levels of portal plasma insulin and circulating serum leptin and induction of acetyl-CoA carboxylase and fatty acid synthase mRNAs in the liver of cafeteria rats, consistent with the reduction of liver lipids. The dietary inulin and clofibrate markedly reduced triacylglycerol levels in serum very low density lipoprotein (VLDL) and liver and epididymal adipose tissue weights of cafeteria rats; the extent of suppression by the dietary inulin was higher than that by clofibrate. No additive or synergistic effect of the dietary inulin and clofibrate was found in decrease in circulating serum VLDL and liver lipid levels. In contrast, the dietary inulin and fluvastatin synergistically reduced serum triacylglycerol and total cholesterol levels. Furthermore, whereas no significant alteration in the baseline expression of CYP2B, CYP2C11, CYP3A and NADPH-cytochrome P450 reductase mRNAs and proteins was found, the baseline expression and induction of CYP4A in response to clofibrate were suppressed by the dietary inulin. The dietary inulin did not affect the fluvastatin-induced alteration.

These observations indicate that the dietary inulin may prevent the development of metabolic disease such as hyperlipidemia and hyperinsulinemia caused by intake of cafeteria diet, in association with suppression of liver lipogenesis.