Dietary Cyanidin 3-*O*-β-D-Glucoside-Rich Purple Corn Color Prevents Obesity and Ameliorates Hyperglycemia in Mice

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ABSTRACT Anthocyanins, which are used as a food coloring, are widely distributed in human diets, suggesting that we ingest large amounts of anthocyanins from plant-based foods. Mice were fed control, cyanidin 3-glucoside-rich purple corn color (PCC), high fat (HF) or HF + PCC diet for 12 wk. Dietary PCC significantly suppressed the HF diet–induced increase in body weight gain, and white and brown adipose tissue weights. Feeding the HF diet markedly induced hypertrophy of the adipocytes in the epididymal white adipose tissue compared with the control group. In contrast, the induction did not occur in the HF + PCC group. The HF diet induced hyperglycemia, hyperinsulinemia and hyperleptinemia. These perturbations were completely normalized in rats fed HF + PCC. An increase in the tumor necrosis factor (TNF)-α mRNA level occurred in the HF group and was normalized by dietary PCC. These results suggest that dietary PCC may ameliorate HF diet–induced insulin resistance in mice. PCC suppressed the mRNA levels of enzymes involved in fatty acid and triacylglycerol synthesis and lowered the sterol regulatory element binding protein-1 mRNA level in white adipose tissue. These down-regulations may contribute to triacylglycerol accumulation in white adipose tissue. Our findings provide a biochemical and nutritional basis for the use of PCC or anthocyanins as a functional food factor that may have benefits for the prevention of obesity and diabetes. J. Nutr. 133: 2125–2130, 2003.

KEY WORDS: • *anthocyanin* • *cyanidin 3-glucoside* • *obesity* • *hyperglycemia* • *body fat*

Anthocyanins are the largest group of water-soluble pigments in the plant kingdom. They are widely distributed in the human diet through crops, beans, fruits, vegetables and red wine (1), suggesting that we ingest considerable amounts of anthocyanins from plant-based daily diets. In general, anthocyanin pigments are stable under acidic conditions, but are unstable and rapidly broken down under neutral conditions (2). Therefore, anthocyanins have not been recognized as a physiological functional food factor (2). However, we demonstrated that anthocyanins have antioxidative and radical-scavenging activities against hydroxyl and superoxide radicals based on in vitro and in vivo studies (3–5). Among the anthocyanins tested, cyanidin 3-*O*-β-D-glucoside (C3G)[2] (**Fig. 1**) showed substantial antioxidative and anti-inflammatory activities in vivo (6–9). These findings suggest that C3G has beneficial effects beyond its antioxidant activity.

Obesity is defined as the accumulation of excess adipose tissue resulting from various metabolic disorders. It is a strong risk factor for hypertension, hyperlipidemia, heart disease and type2 diabetes mellitus (10,11). It is controlled by both genetic and environmental factors. Among the environmental factors, the chronic consumption of a high fat (HF) diet is strongly associated with the development of obesity. HF diet–induced obesity can lead to insulin resistance. Obesity is associated with a decreased capacity of insulin to regulate glucose and lipid metabolism in the peripheral tissues. The increase in adipose tissue is accompanied by elevations of circulating free fatty acids and tumor necrosis factor (TNF)-α levels (12,13). These can inhibit insulin signaling and pancreatic β-cell function (14).

Recently, much attention has been focused on some food factors that may be beneficial in preventing HF diet–induced body fat accumulation and possibly reduce the risk of diabetes and heart disease. Ide et al. (15) showed that sesamin, found in sesame seed, decreases fatty acid synthesis and enhances β-oxidation in rat liver. Murase et al. (16) showed that dietary diacylglycerol suppresses HF diet–induced body fat accumulation in mice. However, there is little evidence that food factors themselves are beneficial for the prevention of obesity and the amelioration of insulin resistance.

The present study was designed to examine the preventive effect of anthocyanin-rich food color on the development of obesity and hyperglycemia induced by feeding a HF diet. No studies exist on a possible antiobesity effect of dietary anthocyanins. "Purple corn color" (PCC) is made from purple corn (*Zea mays* L.). In Japan, ~50,000 kg/y of PCC is used for the

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[2] Abbreviations used: ACC, acetylCoA carboxylase; ACS1, acyl-CoA synthase1; AMPK, AMP-activated protein kinase; BAT, brown adipose tissue; C3G, cyanidin 3-*O*-β-D-glucoside; dNTP, deoxynucleoside triphosphate; FAS, fatty acid synthase; GPAT, glycerol-3-phosphate acyltransferase; HF, high fat; IKKβ, IκB kinase β; NF-κB, nuclear factor-κB; PCC, purple corn color; SREBP-1, sterol regulatory element binding protein-1; TNF, tumor necrosis factor; WAT, white adipose tissue.

0022-3166/03 $3.00
Manuscript received 25 November 2002. Initial review completed 10 January 2003. Revision accepted 7 May 2003.