Effects of green tea and its components on *in vivo* and *in vitro* gene expression

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Green tea is known to have a variety of beneficial effects against cancer, obesity, and cardiovascular diseases. Previously we reported that dietary supplementation of powdered green tea for 7 days reduces the expression of gluconeogenic enzymes [glucose-6-phosphatase (G6Pase) and phosphoenolpyruvate carboxykinase (PEPCK)] in the mouse liver, suggesting its anti-diabetic effect. In the next experiment, we found that the ingestion of catechin-rich green tea beverage (GTB) for 2 weeks in normal rats caused the decrease in the hepatic gene expression of both gluconeogenic enzymes. After 4 weeks, the lower level was maintained in the G6Pase gene expression when compared to that in water-given rats, while up-regulation of the gene expression of PEPCK was noted. Similar effects were also found in the case of the mouse.

In the present study, we examined effects of GTB on rat hepatoma H4IIE cells. The cells were stimulated with dexamethasone and dibutyryl cAMP to induce increased gene expression of gluconeogenic enzymes. Inclusion of GTB in the culture medium caused reduction of up-regulated expression of these genes as well as hepatocyte nuclear factor 4 alpha (HNF4α) gene expression. GTB was fractionated into chloroform-soluble (Fractions I), ethyl acetate-soluble (Fraction II), methanol-soluble (Fraction III) and the residual (Fraction IV) fractions. Fraction II expected to contain catechins caused attenuation of up-regulated gene expression of these genes as well as down-regulation of HNF4α gene expression. Fraction IV caused synergistic action on up-regulation with dexamethasone/dibutyryl cAMP of the PEPCK gene and up-regulated HNF4α gene expression. These results suggest that GTB down-regulated the expression of HNF4α gene to cause the down-regulated gene expression of gluconeogenic enzymes by GTB. It is conceivable that one reason why GTB failed to down-regulate the hepatic PEPCK gene in the previous animal experiments is the presence of component(s) to up-regulate the PEPCK gene expression which could be more effective in an animal body than in the cultured cells.