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Title	Effect of indole-3-carbinol on hepatic drug metabolizing enzyme activities and carcinogenicity : A possible mechanism of cancer prevention by consumption of cruciferous vegetables
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deficient rat models. Accordingly, the result suggested that, in rats, sex-specific GH secretory pattern contributes to the expression of sex-specific constitution of liver microsomal CYP isozymes. On the other hand, the decrease of CYP2E1 and the increase of CYP4A1 observed in low GH rats were not consistent with the changes of these isoforms in other GH deficient model rats. These CYP isozymes are likely to be affected by symptoms of obesity.

By mimicking the neonatal imprinting on wale specific CYP isoform expression by neonatal androgen, rats were administered with benzo(a)pyrene within one day after the birth and at the puberty simulating the long term secretory pattern of androgen. Imprinting effects on the expressions of CYP isoforms were observed after these treatment with benzo(a)pyrene, an exogenous substance. Therefore, it is suggested that capability to induce some CYP isozymes by an inducer might be potentiated synergistically by the pattern of administration that imitate long term secretory pattern of androgen.

Effect of indole-3-carbinol on hepatic drug metabolizing enzyme activities and carcinogenicity — A possible mechanism of cancer prevention by consumption of cruciferous vegetables —

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It is known that daily consumption of vegetables, especially crucifers such as Brussels sprouts, broccoli and cabbage, reduces the risk of developing cancer. Several studies have shown that indole-3-carbinol (I3C), which is a component of cruciferous vegetables, inhibits carcinogenesis in rodents and in trouts. On the other hand, it has also been reported that I3C significantly induces cytochrome P450 (CYP)1A, which is responsible for metabolic activation of several procarcinogens, including polycyclic aromatic hydrocarbons (PAHs) such as benzo(a)pyrene (BP), to ultimate carcinogens.

In order to clarify mechanisms underlying anticarcinogenicity by I3C, we treated male SD rats with I3C by gavage for one week (50 mg/kg/day). It was found that pretreatment of rats with I3C increased both phase I (CYP) and phase II (glutathione S-transferase and UDP-glucuronyl transferase) enzymes. In contrast to the anticarcinogenic effects by I3C in vivo, enhancement of metabolic activation of BP was found in the Ames mutation assay if the carcinogen was preincubated with liver post-mitochondrial supernatant fraction (S9) from I3C treated rats. However, when the carcinogen was preincubated with liver S9 in the presence of cofactors for glutathione S-transferase and UDP-glucuronyl transferase, this enhancement was significantly reduced, indicating that mutagenic intermediates of BP produced by CYP1A were effectively detoxified by phase II enzymes in the liver.

These results, suggested that the simultaneous induction of phase I and phase II enzymes is the mechanism of cancer preventiion by I3C, which would promote the excretion of carcinogens from the body and reduce their exposure time.