[*Jpn. J. Cancer Res.*, **88**, 821-830 (1997)] [Lab. of Biochemistry]

Chemoprevention of Azoxymethane-induced Rat Colon Carcinogeneis by A Xanthine Oxidase Inhibitor, 1'-Acetoxychavicol Acetate.

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The modulating effects of feeding of 1'-acetoxychavicol acetate (ACA) during the initiation and post-initiation phases on azoxymethane (AOM)-induced colon tumorigenesis, were investigated in F344 rats. Feeding of ACA significantly inhibited the development of ACF, the 5'-BrdU labeling index, ODC activity and blood polyamine levels. ACA also elevated the activities of phase II enzymes, glutathione S-transferase (GST) and quinone reductase (QR), in the liver and colon. These results indicate that ACA could inhibit the development of AOM-induced colon tumorigenesis through its suppression of cell proliferation in the colonic mucosa and its induction of GST and QR. The results confirm our previous finding that ACA feeding effectively suppressed the development of colonic ACF. These findings suggest possible chemopreventive ability of ACA against colon tumorigenesis.

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Citrus Auraptene Inhibits Chemically Induced Colonic Aberrant Crypt Foci in Male F344 Rats.

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The modifying effect of dietary administration of auraptene isolated from the peel of citrus fruit (*Citrus natsudaidai* Hayata) on the development of azoxymethane (AOM)-induced colonic aberrant crypt foci (ACF) was investigated in rats. Feeding of auraptene suppressed expression of cell proliferation biomarkers (5-bromo-2'-deoxyuridine labeling-index, ornithine decarboxylase activity, polyamine content and number of silver stained nucleolar organizer region protein particles) and the occurrence of micronuclei caused by AOM. Also, auraptene increased the activities of phase II enzymes (glutathione S-transferase and quinone reductase) in the liver and colon. These findings might suggest that inhibition of AOM-induced ACF may be associated, in part, with increased activity of phase II enzymes in the liver and colon and suppression of cell proliferation in the colonic mucosa.

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Changes in Tissue and Blood Polyamines During *N*-Butyl-*N*-(4-hydroxybutyl)-nitrosoamine-induced Bladder Carcinogenesis in Rats.

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Polyamines are recognized as cell growth factors. The concentrations of three polyamines, diamine, spermidine and spermine, in bladder and blood were determined during N-butyl-N-(4-hydroxybutyl) nitrosoamine (BBN)-induced bladder carcinogenesis in male F344 rats. BBN induced bladder hyperplasia in 4 of 5 rats at 8 weeks, papillomas in 2 of 5 rats at 12 weeks, and transitional cell carcinoma in all rats by 20 weeks. The levels of total polyamine in both bladder and blood of the rats during 12-20 weeks were significantly higher than those of control animals given water alone. The elevation of total polyamine was mainly due to the increase of spermidine of the three polyamines, which was coincident with the incidence of bladder tumors. The results indicated that the polyamines are exellent biochemical markers for bladder tumors.

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Changes in Tissue and Blood Polyamine Levels Following Chemotherapy in Rats with Urinary Bladder Carcinma Induced by *N*-Butyl-*N*-(4-hydroxybutyl)nitrosamine in Rats.

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Polyamines are recognized as cell growth factors. The concentrations of three polyamines, diamine, spermidine and spermine in urinary bladder and blood were determined in male F344 rats with urinary bladder carcinoma induced by N-butyl-N-(4-hydroxybutyl) nitrosamine (BBN), following chemotherapy with cisplatin, methotrexate and pirarubicin. Bladder carcinoma was observed in 5 of 20 rats of the chemotherapeutic group, and in 16 of 20 rats of the control group given saline alone. The levels of spermidine, spermine and total polyamine in both bladder and blood of the treated rats were significantly lower than those of the control rats. The study suggested that the levels of tissue and blood polyamines could be used as biochemical markers for monitoring the efficacy of the chemotherapy for bladder tumors.