

[0-7]

## CHEMOPREVENTIVE EFFECTS OF ETHYL 3-(4'-GERANYLOXY-3-METHOXYPHENYL)-2-PROPENOATE AND FERULIC ACID ON MOUSE COLON CARCINOGENESIS

Beom Seok Han<sup>1</sup>, Dong Whan Shin<sup>1</sup>, Young Na Yum<sup>1,2</sup>, Jeong Sik Cho<sup>1</sup>,  
Ki Wha Yang<sup>1</sup>, Nobuo Takasuka<sup>2</sup>, Tetsuyuki Takahashi<sup>2</sup>, Hiroyuki Tsuda<sup>2</sup>

<sup>1</sup>Division of General Toxicology, National Institute of Toxicological Research

<sup>2</sup>Department of Experimental Pathology and Chemotherapy, National Cancer Center  
Research Institute

Ethyl 3-(4'-geranyloxy-3-methoxyphenyl)-2-propenoate (EGMP) and ferulic acid (FA) have been shown to inhibit development of aberrant crypt foci (ACF) in the azoxymethane (AOM)-treated rat colon. In the present study, inhibitory effects of EGMP and FA on the post-initiation stage of AOM-induced colon carcinogenesis were studied in male ddY mice. The animals were given 6 s.c. injections of AOM (10mg/kg body weight) during a 5 week period and thereafter fed basal diet containing EGMP or FA at concentrations of 1.0% or 0.2% for 21 weeks and then sacrificed. Relative liver weights in the group fed 1.0% EGMP were significantly increased as compared to those in AOM alone group ( $P<0.05$ ). Tumor multiplicity in the large intestine with 0.2% EGMP was significantly decreased (to 46.7% of control value,  $P<0.01$ ). Hyperplasia and adenoma multiplicity of the large intestine were also decreased by 0.2% EGMP as compared to AOM alone group (45.5% and 44.4% of control values,  $P<0.05$  and  $P<0.01$ , respectively). Although not significant, FA showed a tendency to inhibit tumor development in the large intestine. BrdU labeling indices in the surrounding and tumor epithelium of the large intestine with 0.2% EGMP were significantly decreased (73% and 71% of control value,  $P<0.05$  and  $P<0.01$ , respectively). Apoptosis labeling indices in the surrounding and tumor epithelium of the large intestine with 1.0%, 0.2% EGMP and 1.0% FA were significantly increased (to 2.56, 3.94 and 2.78 fold of control value,  $P<0.01$ ,  $P<0.001$ , and  $P<0.05$ ). These findings suggest that EGMP has potential as a chemopreventive agent against colon tumor development.

keyword : Chemoprevention, EGMP, FA, mouse colon carcinogenesis