CHEMOPREVENTIVE PROPERTIES OF NIMESULIDE, A SELECTIVE CYCLOOXYGENASE-2 INHIBITOR, AGAINST PHIP-INDUCED MAMMARY CARCINOGENESIS IN RATS

Toshihiko Kawamori, Seiichi Nakatsugi, Toshihisa Ohta, Takashi Sugimura, Keiji Wakabayashi

Cancer Prevention Division, National Cancer Center Research Institute, 1-1 Tsukiji 5-chome, Chuo-ku, Tokyo 104-0045 Japan

Epidemiological and laboratory animal studies have demonstrated that non-steroidal anti-inflammatory drugs (NSAIDs) reduce the risk of development of several cancers. Nimesulide, a selective cyclooxygenase-2 (COX-2) inhibitor, is a good candidate for chemoprevention against cancers in several organs including colon (Fukutake, *et al.* (1998) *Carcinogenesis* **19**: 1939-1942, Nakatsugi, *et al.* (1997) *Jpn J Cancer Res.* **88**: 1117-1120, Takahashi, *et al.* (1997) *J Cancer Res. Clin. Oncol.* **122**: 219-222) and urinary bladder (Okajima, *et al.* (1998) *Cancer Res.* **58**: 3028-3031). The present study was designed to evaluate its chemopreventive efficacy against 2-amino-1-methyl-6-phenylimidazo[4,5-*b*]pyridine (PhIP)-induced mammary carcinogenesis in female SD rats. Seven weeks old SD female rats were given intragastric injections of PhIP (85 mg/kg body weight) 4 times weekly for 2 weeks and maintained on either control diet (AIN-76A containing 23.5% corn oil) or experimental diet (control diet with 400 ppm nimesulide) throughout the experiment. At week 21, all animals were sacrificed and all mammary tumors were evaluated histopathologically. No differences between the control and experimental diet groups in body weights of rats were observed. The mammary tumor incidence (% animals with tumors) and multiplicity (number of tumors/rat) were 71% and 2.6, respectively, in the control diet group versus 51% and 1.2, respectively, in the experimental diet group. The reduction of mammary tumor multiplicity was significant ($P<0.05$). The results thus suggest that this selective COX-2 inhibitor possesses chemopreventive properties against mammary carcinogenesis as well as colon and urinary bladder carcinogenesis.