1,2-Dichloropropane (1,2-DCP) has been used as an intermediate in production for other chemicals and as a paint remover. IARC reclassified it as carcinogenic to humans (Group 1) according to the epidemiological studies of cholangiocarcinoma among offset color proof-printing workers exposed to 1,2-DCP in Japan. The present study investigated hepatotoxicity and proliferation in the bile duct induced by exposure to 1,2-DCP and role of P450 in its toxicity by inhibiting P450 activity using 1-aminobenzotriazole (1-ABT).

Methods: 42 male C57BL/6J mice were randomly divided into 7 groups of six each. Four groups of mice administrated subcutaneously with 1-ABT at 50mg/kg were exposed to 1,2-DCP at 0, 50, 250 and 1250 ppm, respectively via inhalation route, 8hs per day for 4 weeks. The other three groups administered with saline were exposed to 1,2-DCP at 0, 50 and 250 ppm, respectively. Organ samples were collected under anesthesia at the end of the experiment. BrdU was injected intraperitoneally to the mice one hour prior to dissection for observation of proliferation in bile duct epithelial cells.

Results: Serious hepatic pathological changes were found in the groups of 1250 ppm 1,2-DCP with 1-ABT injection and 250 ppm 1,2-DCP without 1-ABT injection, including massive necrosis, inflammation, and hepatocyte degeneration. BrdU labeling index tended to increase with exposure levels of 1,2-DCP in the groups without 1-ABT treatment, but this increase was suppressed by administration with 1-ABT.

Conclusions: 1-ABT could reduce liver damage induced by 1,2-DCP exposure, indicating that P450 plays an important role in the hepatotoxicity of 1,2-DCP. P450-mediated metabolism of 1,2-DCP might contribute to proliferation in bile duct epithelial cells induced by exposure to 1,2-DCP.