Genotoxic evaluation of Gyllus bimaculatus in 3 sets of mutagenicity tests

Ahn Mi Young°, Pae Hey Jin, Lee Byung Mu, Ryu Kang Sun
Dep. Seri & Entomol, Nat Inst of Agri Sci & Tech, RDA, Div of Toxicol, School of Pharmacy, Sung Kyun Kwan University

The mutagenic potential of Gryllus bimaculatus was evaluated using the short-term genotoxicity tests including Ames, chromosome aberration and micronuclei tests. In salmonella typhimurium assay, G. bimaculatus did not show any mutagenic response in the absence or presence of S9 mix with TA98, TA100, TA1535, and TA1537. In chromosome aberration test, G. bimaculatus did not show any significant effect on Chinese Hamster Ovary (CHO) cells compared with control. In mouse micronucleus test, no significant increase in occurrence of micronucleated polychromatic erythrocytes was observed in ICR male mice intraperitonealy administered with G. bimaculatus at a dose of 15, 150 and 1500 mg/kg. These results indicate that G. bimaculatus has no mutagenic potential in these in vitro and in vivo systems.

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Cytochrome P-450 3A4 proximal promoter activity by histone deacetylase inhibitor in HepG2 cell.

Kim JaYoung°, Ahn MeeRyung1, Sheen YhunYhong
Ewha Womans University, College of Pharmacy, National Institute of Toxicological Research, Korea Food & Drug Administration1

Cytochrome P-450 3A4 (CYP3A4) is major enzyme in human liver, the role of this is detoxification and metabolizing more than 50% clinical drugs in use. Expression of CYP3A4 is transciptionally regulated by the Pregnenolone X receptor (PXR), of which human form is Steroid and Xenobiotics receptor (SXR). SXR is activated by wide range of endogenous and exogenous compounds, and then induces CYP3A4 gene expression. In the previous study, it has been known that proximal promoter (-864 to +64) does not response to chemical inducers such as pregnenolone 16a-carbonitrile (PCN), Rifampicin, Estrogen in terms of transcription of CYP 3A4 in cultured cells. Here, we developed luciferase reporter gene assay system to detect SXR-based CYP 3A4 transcriptional activity. We have used CYP3A4-Luc plasmid that contains proximal promoter of human CYP3A4 gene upstream of the luciferase gene. We did transient transfection of 3A4-luciferase gene and SXR. In the HepG2 cells transfected with CYP3A4-Luc, when rifampicin treatment was combined with histone deacetylase inhibitor (HDAC Inhibitor), such as Trichostatin A, Hc-toxin and IN 2001 of the luciferase activity was induced 10-20 fold over control.

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Induction of apoptosis by dihydro-N-caffeoyltyramine on human leukemia cells

Choi Chul Yung°, Kim Ji Young, Lee Kyung Jin, Oh Duk-Hee, Han Song-Hee, Woo Eun-Rhan, Jeong Hye Gwang
Division of Food Science, Jinju International University, Jinju, Korea, Department of Pharmacy and Research Center for Proteineous Materials, Chosun University, Kwangju, Korea

Lycii Radicis Cortex, the root bark of Lycium chinense Miller (Solanaceae) is used in oriental medicine as a tonic and is reported to exhibit hypotensive, hypoglycemic, and antipyretic activity. Recently, we have isolated dihydro-N-caffeoyltyramine, a phenolic amide, from the Lycii Radicis Cortex. Treatment with dihydro-N-caffeoyltyramine significantly inhibited the proliferation of human leukemia cell lines HL-60 in a dose-dependent manner. We found also that the growth inhibition of HL-60 by dihydro-N-caffeoyltyramine is associated with induction of apoptosis of cells. Dihydro-N-caffeoyltyramine induced the apoptosis of HL-60 such as apoptotic body and DNA fragmentation. In addition, the flow cytometric analysis revealed dihydro-N-caffeoyltyramine dose-dependently increased apoptotic cells with hypodiploid DNA contents. These results indicate that 4372 can control growth of leukemic HL-60 cells through apoptosis and may have a possibility of