TURJOEM
The Turkish Journal of Occupational / Environmental Medicine and Safety

Vol:2, No:1 (1), 2017 Web: http://www.turjoem.com ISSN : 2149-4711

SHC 15. CYP1B1 AS A THERAPEUTIC TARGET FOR ANTICANCER DRUGS

Elif INCE, Alev TASCIOGLU, Çigdem KARAASLAN, Natalia BILARDI, Sibel SUZEN, Hande Gurer-ORHAN

Department of Pharmaceutical Toxicology, Faculty of Pharmacy, Ege University, 35100, Izmir, Turkey

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Ankara University, Tandogan-06100, Ankara, Turkey

[+]Erasmus + programme exchange student from Catania University Faculty of Pharmacy

Most of the known carcinogens are known to be procarcinogens which are metabolized to ultimate carcinogens in the body and CYP1 enzymes are major catalysts in this bioactivation reactions. Especially CYP1B1 is very active in catalyzing the bioactivation of carcinogens like benzo[a]pyrene, dimethylbenzanthracene and also endogenous estrogens. Therefore CYP1B1 inhibition seems to be a promising target as a strategy for cancer prevention and therapy. Since melatonin -a natural indolic hormone which mainly synthesized in pineal gland- shows chemopreventive activity by inhibiting procarcinogen bioactivating CYP1 enzymes, we have synthesized series of 5-metoxyindole-3-aldehyde hydrazone derivatives and investigated their potential inhibitory effects on catalytic CYP1B1 activity via EROD assay. The results indicated that newly synthesized compounds strongly inhibited hepatic microsomal CYP1 activity while mono halogenated compounds have potently inhibited human recombinant CYP1B1 activity. Position of the halogenation did not effect the inhibitor activity. Among mono halogenated derivatives, *o*-chloro substituted one was found to be more potent (IC_{50}=11nM) than specific CYP1B1 inhibitor, alizarin. In conclusion, our compounds seems to be promising candidates for preventing CYP1B1 mediated carcinogenesis process.

This work was supported by The Scientific and Technological Research Council of Turkey (TÜBİTAK) Grant 112S599. *Enzyme activity studies are performed at Ege University Faculty of Pharmacy Pharmaceutical Sciences Research Center (FABAL).*

* ecz.elifince@gmail.com