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MEETING ABSTRACTS

THE HEPATOTOXICITY OF HELENALIN IN DIFFERENTIATED HEPARG CELLS

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Helenalin (HEL) is a sesquiterpene lactone used as an antiphlogistic in European and Chinese folk medicine. Its characteristic anti-inflammatory activity is mediated by direct alkylation of Cys38 within the DNA binding domain of NF-κB subunit p65/RelA. In addition, HEL is a broad-spectrum active compound, featuring an antitumor, antibacterial, and antiprotozoal activity. Recently, a new interest in the biological and pharmacological activities of HEL or its synthetic analogs has been observed (1). HEL has been found to undergo oxidative as well as reductive biotransformation in human liver. In addition, HEL acted as a mechanism-based inhibitor of human cytochrome P450 enzymes (2). Yet, information concerning its potential hepatotoxicity in human is limited. To address this issue, the hepatotoxic effect of HEL was studied in differentiated HepaRG cells that represent a human hepatocytes-like model. Firstly, the cytotoxic effect of HEL was determined using neutral red uptake (NRU) and MTT assay. After 72-hour incubation, the half-maximal inhibitory concentration (IC_{50}) of HEL was 13 μM and 11 μM using NRU and MTT assay, respectively. Secondly, the pro-oxidant activity of HEL was assessed using oxidant-sensitive probe. HEL was found to increase the formation of reactive oxygen species in a time- and concentration-dependent manner. Thirdly, a comprehensive proteomic analysis using isobaric labeling was performed to study the changes in hepatic proteome upon HEL treatment.

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Keywords: helenalin; HepaRG; hepatotoxicity; reactive oxygen species; proteomics

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