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Effects of Ibuprofen and Indomethacin on ALDH3A1 Induction by 3-Methylcholanthrene

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AIM

A number of various physiological and pathophysiological roles have been reported for the induced enzyme activities of a group of aldehyde dehydrogenases. In the present study, the effects of co-administration of a non steroidal antiinflammatory drug (ibuprofen or indomethacin) and a polycyclic aromatic hydrocarbon (3-methylcholanthrene, 3MC) in human hepatoma cells were examined.

METHODS

The expression of the enzyme aldehyde dehydrogenase 3A1 (ALDH3A1) was studied in this cell line, after exposure firstly to ibuprofen or indomethacin and then to 3MC. The in vitro toxicity of the above substances was also studied by using the WST-1 toxicity test. WST-1 is a reliable test for the study of the viability/proliferation capacity of the cells based on the cleavage of the tetrazolium salt WST-1 to formazan by mitochondrial enzymes of the living cells. Different concentrations of the drugs or of 3MC were used for the exposure of the cells during several time periods.

RESULTS

Exposure of the cells to 3MC, showed typical time- and dose-response curves of induction. When the cells were firstly exposed to ibuprofen or indomethacin (5 days) and then to 3MC (3 days), a statistically significant decrease in ALDH3A1 inducibility was observed, compared to the application of 3MC alone for the same time period.

CONCLUSIONS

Even if the mechanism of decrease of ALDH3A1 inducibility remains unknown, the effects of the non steroidal anti-inflammatory drugs on the induction of drug metabolizing enzymes from carcinogens, is an interesting finding.