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Antioxidant effects of ursodeoxycholic acid in doxorubicin-induced oxidative hepatocyte injury

Bojan Stanimirov, Karmen Stankov, Nebojša Pavlović, Maja Đanić, Svetlana Goločorbin-Kon, Velibor Vasović, Momir Mikov

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syndrome. Chemical sensitizers react non-specifically with cellular molecules. Responses are activated after a certain threshold of insults is exceeded. Exposure to VOC may cause changes in metabolism long before obvious allergic signals manifest. Thus, there is an urgent need to identify pathways that (i) are affected at low, sublethal VOC concentrations and (ii) have a functional connection to the development of above-mentioned effects. These requirements are met by the immunoregulatory pathway of indoleamine 2,3-dioxygenase (IDO-1)-mediated tryptophan breakdown.

We investigated the effect of common indoor air pollutants such as formaldehyde and terpenes limonene and pinene on tryptophan breakdown in human peripheral mononuclear cells in the presence or absence of inflammatory stimuli. We show that IDO-1 activity was more sensitively suppressed with all airborne sensitizers in mitogen-stimulated compared to unstimulated cells. Moreover, the inhibition was dose-dependent and occurred already at sublethal concentrations. Data suggest that antioxidative capacity of the above mentioned compounds favors a reductive milieu, suppressing immunobiochemical pathways such as IDO-1 activity. Dysregulation of this first essential step in tryptophan metabolism has manifold consequences, as several downstream products exert bioactivities in the regulation of immunological, stress response and neurological processes.

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P-12-00-08 Antioxidant effects of ursodeoxycholic acid in doxorubicin-induced oxidative hepatocyte injury

Bojan Stanimirović1,*, Karmen Stankov1, Nebojša Pavlović2, Maja Đanić1, Svetlana Goločorbin-Kon2, Velibor Vasočić3, Momir Mikov3

1 Department of Biochemistry, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia
2 Department of Pharmacy, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia
3 Department of Pharmacology, Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia

Doxorubicin (D) is a potent anticancer drug; however, hepatotoxicity commonly overshadows its anti-neoplastic effectiveness. The overproduction of free radicals is considered as a significant cause of this side effect. The aim of the study was to evaluate influence of ursodeoxycholic acid (U) on lipid peroxidation (LPO) and expression of glutathione-dependent antioxidative enzymes in the livers of rats treated with D. Male Wistar rats were divided into 3 groups and administered with saline i.p. (K), 3 mg/kg i.p. of D every other day for total 3 doses (D) or combined with U 25 mg/kg p.o. every other day for total 3 doses between administering D (DU). On the day 28 animals were euthanized. In the livers of animals administered with D, LPO was slightly increased compared to control, whereas in DU group LPO was close to control values. Treatment with D increased specific activities of glutathione peroxidase compared to control (p = 0.01) and decreased in DU group but non-significantly compared to D. The activity of glutathione reductase was non-significantly increased in both experimental groups but slightly reduced compared to D. Specific activity of glutathione-S-transferase was increased in D and DU groups (p = 0.01, p = 0.04, respectively). Ursodeoxycholic acid represents an agent with potentially hepatoprotective properties against oxidative liver damage induced by high doses of doxorubicin. Acknowledgment: Supported by HORIZON2020 MEDLEM project No.690876, and the Project for Scientific and Technological Development of Vojvodina No.114-451-2072-/2016-02.

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P-12-00-09 Organ toxicity attenuation by nanomicelles containing curcuminooids: Comparing the protective effects on tissues oxidative damage induced by Diazinon

Hamidreza Mohammadi

Department of Toxicology and Pharmacology, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran, Sari, Islamic Republic of Iran

Diazinon (DZ) is an organophosphate pesticide that induces oxidative damage in different organs. The aim of this study is comparing the effectiveness of nanomicelles containing curcuminoids (NCUR) and natural curcumin (CUR) on attenuation of oxidative damage induced by DZ in male rats. After a single intraperitoneal (ip) injection of DZ (100 mg/kg), CUR (25 and 60 mg/kg) and NCUR (25 and 60 mg/kg) were administered (ip). Oxidative damage biomarkers including, Alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), creatinine (Cr), urea, lactate dehydrogenase (LDH), Creatine Kinase MB isoenzyme (CK-MB) and troponin I were detected in serum. Lipid peroxidation (LPO) and glutathione content (GSH) in the liver, kidney and heart tissues were determined. Elevated serum levels of ALT, AST, ALP, Cr, urea, LDH, CKMB and troponin I following DZ administration were significantly decreased after treatment by CUR and NCUR. LPO and GSH significantly improved by NCUR at all doses when compared with CUR. Our findings suggest that NCUR treatment has more protective effects to attenuate oxidative damage induced by DZ. It can be suggested that synthesized NCUR, with high blood circulation, can quench the free radicals and prevents or excises the oxidative damage processes and attenuates the oxidative tissues damage.

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P-12-00-10 Improved IC-50 prediction using the Quasi Vivo® in vitro dynamic cell culture flow system

John Malcolm Wilkinson*, Kelly Davidge

Research and Development, Kirkstall Ltd., Rotherham, United Kingdom

There is currently interest in the construction of complex in vitro models with the eventual goal of simulating the behaviour of an organ or even a whole organism. Our gold standard for clinical response is the human body. It is now recognised that 3D cell cultures are more representative of human physiology than 2D monolayers of cells growing on a flat surface. Correct organ function also requires gradients of oxygen and metabolites and removal of waste material, as well as co-culture of multiple cell type. To accurately mimic clinical behaviour, cells should be in a 3D environment and provided with a physiologically-relevant flow of media. Past workers have shown that primary hepatocytes cultured in a collagen sandwich show more human-like expression of key detox genes (Vinci et al., 2011) and fibroblasts cultured under flow show vastly different gene expression profiles compare with those cultured in static conditions (Nithiananthan et al., 2016).