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MEETING ABSTRACTS

IN VITRO DETERMINATION OF OXIDATIVE STRESS INDUCED BY OXIME REACTIVATORS USING CHROMATOGRAPHIC METHODS

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Even though reactive oxygen/nitrogen species (ROS/RNS) are physiologically generated in biological systems, their excessive production may cause severe damage of cellular components. Excessive production of ROS/RNS can occur in response to various stressors such as xenobiotics, radiation or pathological processes. Oxidative stress has also been reported to cause adverse effects of some therapeutic drugs including acetylcholinesterase (AChE) oxime reactivators which are used in therapy of organophosphate poisoning.

In this study, we determined the effect of obidoxime, methoxime, asoxime, pralidoxime and trimedoxime on redox homeostasis in cultured human hepatoma (HepG2) cells. The cells were incubated with oximes at concentration corresponding with their IC_{50} for 1, 4 and 24 hours. Intracellular ROS levels were determined using two fluorescent probes (2',7' dichlorodihydrofluorescein diacetate and dihydroethidium). Malondialdehyde and 3 nitrotyrosine were measured using LC-MS/MS. Additionally, non-protein thiols and non-protein disulfides were evaluated to reflect antioxidant capacity. Individual reactivators displayed distinct quantitative and/or qualitative changes in redox homeostasis reflecting different role of oxidative stress in their intrinsic toxicity. Future perspectives are to test new AChE reactivators synthetized at Department of Toxicology and Military Pharmacy in order to minimalize their unwanted side effect related to oxidative stress.

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