

the alteration of hormone transport kinetics through the rate controller membrane of intra uterine therapeutic systems having calcified deposits (incrustments) on their surface. The formation of incrustments was visualized by scanning electron microscopy and their composition was determined by energy dispersive x-ray spectroscopy. Based on the visually observed thickness of incrustment layers, and the amount of incrustments on the membrane surface, the model enables the calculation of the reduced diffusion coefficient, thus the delay of the hormone release. The in utero growth of the incrustments should be periodically monitored by the noninvasive ultrasonic technique to avoid the ineffective hormone release and harmful physiological effects.

755. VARIATIONS IN ACETYLCHOLINESTERASE AND PROTEIN LEVELS IN HUMAN BLOOD SAMPLES TREATED WITH LOW DOSES OF SOME ORGANOPHOSPHORUS PESTICIDES: IN VITRO STUDIES

Prabhavathy G. Das and Kaiser Jamil*

Department of Genetics, Bhagwan Mahavir Medical Research Centre, Masab Tank, Hyderabad Andhra Pradesh, India

The relative toxicity of three Organophosphorus pesticides namely Chlorpyrifos (CLP), Monocrotophos (MCP) and Acephate (ACP) on Acetylcholinesterase (AChE) and total blood proteins was estimated in vitro on the peripheral blood samples of healthy human donors. As the concentration (0.2–1.0 mg/ml for CLP and MCP and 2.0–10 mg/ml for ACP) and time of exposure to pesticides increased, the inhibition also increased in a dose-dependent manner. An increase in total blood proteins (from 7.3 ± 0.223 gm/dl to 8 ± 0.287 gm/dl) at lower concentrations of pesticide treatment followed by a subsequent decrease at higher concentrations (7.3 ± 0.223 gm/dl to 6.2 ± 0.278 gm/dl) of the pesticides was very interesting. At LD₅₀ doses of exposure of CLP, MCP and ACP (0.75, 1.0 and 6.5 mg/ml respectively), a decrease in total protein (7.3 ± 0.223 gm/dl to 6.8 ± 0.402 gm/dl) and albumin levels (5.7 ± 0.460 gm/dl to 3.2 ± 0.402 gm/dl) but an increase in globulin fraction (2.5 ± 0.502 gm/dl to 3.6 ± 0.492 gm/dl) was observed. AChE was inhibited at all the treated concentrations. Based on IC₅₀, CLP was found to be a potent inhibitor followed by MCP whereas ACP was the least inhibitor of AChE at 15' exposure time (0.128 ± 0.088 , 0.225 ± 0.143 and 4.03 ± 0.538 mg/ml respectively). All the results were statistically evaluated and were significant ($p < 0.001$, ANOVA). These studies provide a valuable insight into the mechanism of action of the pesticides in vitro. Hence, it is evident that in vitro methods being sensitive and easy to handle with great amount of reproducibility can be used for evaluating any number of chemicals or drugs for toxicity studies. Very low doses of the pesticides (1/10th of LC₅₀) can induce these changes, making it possible for early detection of the dangers of chemical exposures. Inhibition of AChE and blood proteins can be used as biomarkers both in field workers and laboratory conditions.

756. EFFECT OF DELTAMETHRIN ON GENE EXPRESSION OF BOTH GAMMA-GLUTAMYL CYSTEINE SYNTHETASE AND NRF2 IN BRAIN TISSUE

Li Huangyuan^{1,*}, Shi Nian¹, Dai Zhonghua, Zhong Yufang¹, and Ma Qiang^{*2}

¹Department of Health Toxicology, School of Public Health, Huazhong University of Science and Technology, Wuhan, China 430030; ²Receptor Biology Laboratory, Toxicology and Molecular Biology Branch, NIOSH/CDC, Morgantown, WV 26505, USA

Recent studies show that activation of transcriptional factors NF-E2 related factor 2 (Nrf2) is a key initiation step in the cellular response against chemical stress and Nrf2 involves in the regulation of expression of gamma-glutamylcysteine synthetase heavy (GCSH) and light subunit (GCSI). To our knowledge, however, there is no study reported whether disruptions in Nrf2 and GCS occur in oxidative stress induced by Deltamethrin (DM). Wistar male rats were administrated (daily dose is respectively 0, 3.1, 12.50 mg/Kg BWT) with i.p. for five days. The relative amount of mRNA expression of genes was measured by RT-PCR. The protein level was immunohistochemistry detected. There was no effect on mRNA expression level of GCSH and Nrf2 gene in both cerebral cortex and hippocampus tissue in rats administrated with DM. However, the mRNA level of GCSI gene in cerebral cortex of high dose group as well as in both cerebral cortex and hippocampus of low dose group was significantly lower than that in corresponding tissue of control group, decreased to 71.1%, 63.6%, and 75.2% of mRNA level of corresponding tissue of control group ($P < 0.001$). There was no obvious effect on protein level of both GCSH and Nrf2 in hippocampus as well as on that in cerebral cortex in rat treated with DM [supported by National Natural Science Foundation in China (30371225)].

757. TIME COURSE OF GENE EXPRESSION OF GAMMA-GLUTAMYL-CYSTEINE SYNTHETASE SUBUNIT AND NRF2 IN BRAIN TISSUES OF RATS TREATED WITH DELTAMETHRIN

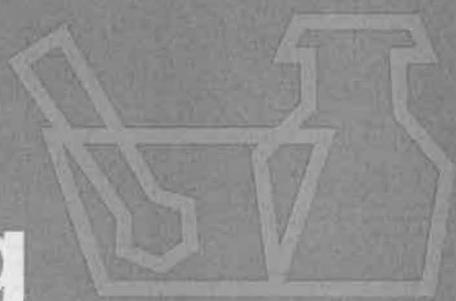
Li Huangyuan^{*.1}, Shi Nian¹, Dai Zhonghua, Zhong Yufang¹, and Ma Qiang^{*.2}

¹Department of Health Toxicology, MOE Key Laboratory of Environment and Health School of Public Health, Huazhong University of Science and Technology, Wuhan China 430030; ²Receptor Biology Laboratory, Toxicology and Molecular Biology Branch, NIOSH/CDC, Morgantown, WV 26505, USA

Recent studies show that activation of transcriptional factors Nrf2 is a key initiation step in the cellular response against chemical stress and Nrf2 involves in regulation of expression of gamma-glutamylcysteine synthetase heavy (GCSH) and light subunit (GCSI). To our knowledge, however, there is no study reported whether disruptions in Nrf2 and γ -GCS occur in neurotoxicity induced by Deltamethrin (DM). Wistar male rats were administrated with DM (single dose is respectively 0, 12.50 mg/Kg BWT) with i.p. for one time. At various time points post-exposure, the relative amount of mRNA expression of these genes was measured by the method of RT-PCR and the protein level was detected by the method of immunohistochemistry and image analysis system. After single dose of DM exposure, there are up-regulation of mRNA expression of both GCSH and GCSI gene in rats hippocampus, down-regulation of mRNA expression of GCSH gene and up-regulation of mRNA expression of Nrf2 gene in rats cerebral cortex under the experimental condition. However, there is no obvious change on protein level of both GCSH and Nrf2 in hippocampus and cerebral cortex [supported by National Natural Science Foundation in China (30371225)].



Official Journal of the International Society
for the Study of Xenobiotics (ISSX)



Drug Metabolism Reviews

Biotransformation and Disposition of Xenobiotics

executive editor

JACK A. HINSON

ABSTRACTS FROM
13TH NA ISSX / 20TH JSSX MEETING

October 23–27, 2005
Maui, Hawaii

Volume 37

Supplement 2

2005



Taylor & Francis
Taylor & Francis Group