



**10th Congress of Toxicology
in Developing Countries (CTDC10)**
**12th Congress of the Serbian Society
of Toxicology (12th SCT)**

BOOK OF ABSTRACTS

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Oximes keep their place in the treatment of acute intoxication with cholinesterase inhibitors. Their indication should be discussed for each case by taking into account the anamnesis, clinical picture and rate of cholinesterase activity.

Keywords: pesticides, pralidoxime, organophosphate, carbamate, cholinesterase activity

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S-metolachlor: Acute and Subacute Effects on Common Carp (*Cyprinus carpio* L.)

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Toxicological assessment of S-metolachlor, synthetic organic herbicide frequently used for efficient weeds control, was the subject of the present study. Two exposure experiments (acute - 4 day and subacute - 28 days) were conducted on five months old common carp originated from the same family from the selective breeding program. 96h LC₅₀ was calculated to be 16.31 mg L⁻¹, which is generally high value, since environmental concentrations of S-metolachlor are usually determined to be below 1 mg L⁻¹. Concerning this, three concentrations were set for a subacute test, carried out in triplicates: C0 - 0.0 mg L⁻¹, C1 - 0.5 mg L⁻¹, C2 - 1.4 mg L⁻¹, C3 - 4.1 mg L⁻¹. Biomarkers used for the assessment of fish health status were: histopathology of gills and liver, as well as nuclear abnormalities on erythrocytes. Histological assessment found a number of alterations in both sampled tissues: hyperaemia, presence of eosinophilic granular cells, epithelial lifting, hyperplasia of epithelial cells and focal necrosis in gills; leukocyte infiltration, hyperaemia, fibrosis of blood vessels and focal necrosis in liver. Only two of all mentioned alterations (epithelial lifting and gills hyperemia) had higher levels in the control, while majority were absent from control group. Different morphological abnormalities were noticed on the erythrocyte nuclei: micronucleus, nuclear buds, fragmented-apoptotic, and bi-nucleated cells. Almost all alterations, either histopathological or nuclear, were higher compared to control, but due to the high variation in between groups, statistical significance was not established.

This study confirms low toxicity of S-metolachlor to common carp.

Keywords: herbicide, histopathology, gills, LC₅₀, erythrocytes

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Post-exposure Treatment with the Oxime RS194B Rapidly Reactivates Brain Acetylcholinesterase Activity in Mice Exposed to Sarin and VX

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Acetylcholinesterase (AChE) has a vital function in cholinergic neurotransmission but is irreversibly disrupted after exposure to organophosphate (OP) nerve agents, resulting in onset of toxicity symptoms which may lead to death. Currently used therapy consists of quaternary pyridinium aldoximes as reactivators of inhibited AChE, given along with atropine. The permanent cation precludes these reactivators rapidly crossing the BBB in appreciable concentrations to reactivate synaptic AChE, thereby restricting their activity to the periphery. Alternatives encompass oximes lacking a permanent cationic charge or presenting a tertiary amine as found in the zwitterionic hydroxyiminoacetamido alkylamines (RS194B). We have shown RS194B to be an effective *in vitro* reactivator of human AChE inhibited by VX, sarin, other methylphosphonates and various alkylphosphorates. Here we examine the pharmacokinetic properties, oral bioavailability and antidotal efficacy of RS194B against OP exposure in mice. The results show that 2 h sequential administrations out to 10 h result in steady-state plasma and brain levels of the oxime. Moreover, within the 40 min period brain concentrations of RS194B exceed the plasma concentrations prior to the next administration. Also, RS194B substantially protected mice when administered by gastric lavage prior to OP exposure, whereas 2-PAM exhibited no protection when similarly administered. Furthermore, the observed recovery of the mice brain activity after administering RS194B after exposure to both, VX and sarin is consistent with its rapid tissue disposition and BBB penetration. Those results, along with low

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