

## MEETING ABSTRACTS

## OXIDATIVE STATUS ASSESSMENT OF RATS' BRAIN INJURY FOLLOWING SUBACUTE EXPOSURE TO K-OXIMES

Jelena Dumanović <sup>1,2</sup>, Jelica Grujić-Milanović <sup>3</sup>, Zoran Milovanović <sup>4</sup>, Ljiljana Amidžić <sup>5,6</sup>, Nataša Vojinović <sup>5</sup>, Lana Nežić <sup>7</sup>, Petar Milosavljević <sup>8</sup>, Eugenie Nepovimova <sup>9</sup>, Kamil Kuča <sup>9</sup>, Vesna Jaćević <sup>2,9,10,\*</sup>

Presenting author: Vesna Jaćević (v jacevic@yahoo.com)

- <sup>1</sup> Faculty of Chemistry, University of Belgrade, Studenski trg 16, 11000 Belgrade, Serbia
- <sup>2</sup>Medical Faculty of the Military Medical Academy, University of Defence, Crnotravska 17, 11000 Belgrade, Serbia <sup>3</sup>University of Belgrade, Institute for Medical Research, National Institute of the Republic of Serbia, Department for Cardiovascular Research, Bulevar Oslobođenja 18, 11 000 Belgrade, Serbia
- <sup>4</sup> Special Police Unit, Ministry of Interior, Trebevićka 12/A, 11 030 Belgrade, Serbia
- <sup>5</sup> Center for Biomedical Research, Faculty of Medicine, University of Banja Luka, Save Mrkalja 14, 78000 Banja Luka, Bosnia and Herzegovina
- <sup>6</sup> Institute of Pathology, University Clinical Center of Republic of Srpska, Faculty of Medicine, University of Banja Luka, Beba 12, 78000 Banja Luka, Bosnia and Herzegovina
- Department of Pharmacology, Toxicology and Clinical Pharmacology, Faculty of Medicine, University of Banja Luka, Save Mrkalja 14, 78000 Banja Luka, Bosnia and Herzegovina
- <sup>8</sup> Veterinary Services Center, Military Health Department, Crnotravska 17, 11000 Belgrade, Serbia
- <sup>9</sup> Department of Chemistry, Faculty of Science, University of Hradec Kralove, Rokitanskeho 62, 500 03 Hradec Kralove, The Czech Republic
- <sup>10</sup>Department for Experimental Toxicology and Pharmacology, National Poison Control Centre, Military Medical Academy, Crnotravska 17, 11000 Belgrade, Serbia

In this study, it has been investigated the oxidative status and morphological alterations in the brain of Wistar rats induced by repeated application of low doses of selected acetylcholinesterase reactivators - asoxime, obidoxime, K027, K048, K074, and K075. Each oxime (0.1 of LD50/kg im) was given 2 times per week for 4 weeks. The animals' whole-body, organ weight, oxidative status, as well as microscopic examination of the brain, were done on day 35 of the study. Markers of oxidative stress, lipid peroxidation (malondialdehyde (MDA) and advanced oxidation protein products (AOPP)), as well as the activity of antioxidant enzymes (catalase (CAT) and superoxide dismutase (SOD)), were measured in the brain homogenates (1,2). Brain alterations were quantified by semiquantitative grading scales – brain damage score (BDS) (3). Oxidative stress parameters MDA and AOPP were significantly elevated in the K075-treated group compared to the control group (p < 0.001). SOD activity was significantly higher in the K075-treated group (p < 0.001), without differences in CAT activity. In the same groups of rats, brain injuries were significantly more severe than those observed in animals receiving only asoxime or K027 (p < 0.001). Our results can help to predict likely adverse systemic toxic effects, and target organ systems, which are crucial for establishing risk categories, as well as in dose selection of K-oximes as drug candidates. (MFVMA01/23-25).

Keywords: oximes; toxicity; pathohistology; brain; oxidative stress

## References

1. Bruic M, Grujic-Milanovic J, Miloradovic Z, Jovovic D, Zivkovic L, Mihailovic-Stanojevic N, Karanovic D, Spremo-Potparevic B. DNA, protein and lipid oxidative damage in tissues of spontaneously hypertensive versus normotensive rats. The International Journal of Biochemistry & Cell Biology. 2021;141:106088.

- 2. Grujić-Milanović J, Jaćević V, Miloradović Z, Jovović D, Milosavljević I, Milanović SD, Mihailović-Stanojević N. Resveratrol Protects Cardiac Tissue in Experimental Malignant Hypertension Due to Antioxidant, Anti-Inflammatory, and Anti-Apoptotic Properties. International Journal of Molecular science. 2021;22(9):5006.
- 3. Jaćević V, Nepovimova E, Kuča K. Acute toxic injuries of rat's visceral tissues induced by different oximes. Scientific Reports 2019;9:16425.