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BOOK OF ABSTRACTS

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C-YPP22. STUDY ON THE NEUROPROTECTIVE AND ANTIOXIDANT PROPERTIES OF NEW BENZIMIDAZOLE HYDRAZONES ON SYNAPTOSOMES

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The high sensitivity of neuronal cells to oxidative stress is determined by different factors including stronger dependence on oxidative phosphorylation for energy in comparison to other cells; exposure to high oxygen concentration; metal ions accumulating in the brain with aging that can be a potent catalyst for oxidative species formation and also they are rich in polyunsaturated fatty acids that are prone to oxidation. At the same time they contain relatively poor concentrations of antioxidants.

Oxidative stress is connected with the pathogenesis of many diseases like neurodegenerative disorders such as Parkinson's and Alzheimer's disease.^{1,2} During the progression of neurodegenerative conditions, the capacity of cells to maintain the redox balance decreases, leading to the accumulation of free radicals, mitochondrial dysfunction, and neuronal injury.

In experimental toxicology *in vitro* systems play an important role for the investigation of xenobiotic biotransformation and reveal the possible mechanisms of toxic stress and its protection. The isolated rat brain synaptosomes were treated with 6-hydroxydopamine which is a convenient *in vitro* sub-cellular system for the investigation of processes, which play role in the neurodegenerative diseases, including Parkinson's disease. The mechanism of 6-OHDA neurotoxicity includes the formation of reactive oxygen species and other metabolites, as a result of its metabolism in mitochondria of the nerve cells.

Melatonin has been widely known for its potent antioxidant and neuroprotective action.³ In the present study we are investigating N,N'-disubstituted benzimidazole-2-thione hydrazones synthesized as melatonin analogues for neuroprotective potential. The administered compounds (250 µM) revealed statistically significant neurotoxic effects on isolated rat brain synaptosomes. With lower toxicity were three of the compounds, containing hydroxyl phenyl moieties, which were investigated on 6-hydroxydopamine-induced oxidative stress. The hydrazone bearing a vanillin moiety exhibited the most potent neuroprotective and antioxidant activity, comparable to melatonin.

Keywords: neuroprotection, antioxidants, benzimidazoles, melatonin, synaptosomes

References

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