

Abstract

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Title of diploma thesis: Monitoring the antioxidant activity of newly synthesized potential acetylcholinesterase modulators.

The theoretical part of the diploma thesis focuses on the characteristics of oxidative stress (OS) and antioxidant protection of the organism. In the next part, neurodegenerative diseases and the importance of OS in their development are discussed in detail. In the experimental part, the cytotoxicity of new potential acetylcholinesterase modulators was evaluated using the neuroblastoma cell line SH-SY5Y. The cytotoxicity of the compounds, expressed as IC_{50} , was measured by a colorimetric method using the tetrazolium salt (MTT). This method was also used to determine the maximum tolerated concentration (MTC). These values were subsequently validated by measuring the apoptotic profile of cells in a physiological environment (without OS) and hydrogen peroxide (H_2O_2)-induced OS using microcapillary flow cytometry. The results showed that the compounds did not induce any statistically significant change in the distribution of cells in each population. Subsequently, the antioxidant potential of the individual compounds was monitored. The dihydroethidium (DHE) fluorescent probe was used for this purpose. OS was stimulated with H_2O_2 . The cells were incubated with the compounds and with H_2O_2 for 4 hours. After this time, DHE was added, and the cells were further incubated for 45 minutes. Subsequently, the fluorescence intensity was measured. The results showed that compounds containing secondary amine in their molecule induced a statistically significant decrease in fluorescence. The compounds with antioxidant potential are K2104, K2109, K2133, K2138, K2223, K2247, and K2252.

Keywords: oxidative stress, antioxidant activity, neurodegenerative diseases, cytotoxicity, maximum tolerated concentration, acetylcholinesterase modulators