

## Abstract

Charles University in Prague, Faculty of Pharmacy in Hradec Králové

Department of Biological and Medical Sciences

Candidate Bc. Nikola Žárská

Supervisor PharmDr. Miroslav Kovařík, Ph.D.

Consultant Mgr. Martina Hrabínová

Title of Thesis A comparison of lethal and maximum tolerated dose of standard acetylcholinesterase reactivators.

Diploma thesis deals with the topic of nerve agents. Specifically, it demonstrates the reactivating effect of oxime HI-6 (at 100 % maximum tolerated dose and 5 % median lethal dose) on the acetylcholinesterase inhibited by sarin. The experiment was carried out *in vivo* in Balb/c mice. The treatment was administered either with oxime HI-6 alone, in the above-mentioned doses, or in combination with the parasympatholytic atropine. The change in activity of acetylcholinesterase was measured by spectrophotometrically method, modified by the Ellman, in blood and brain. There were no signs of sarin intoxication in mice, that where treated with 100 % maximum tolerated dose of HI-6, in compare to mice treated with atropine only and 5 % median lethal dose of HI-6, where the intoxication was observed. It was founded that after *i.m* administration of 100 % maximum tolerated dose, the HI-6 concentration reached 500  $\mu\text{M}$  in plasma and 10  $\mu\text{M}$  in brain. This concentration is safe, but for medical purpose irrelevant because it causes mild to moderate side effects.