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Titel des Beitrags: Comparison of the oxime-induced reactivation of erythrocyte and muscle acetylcholinesterase following inhibition by sarin or paraoxon, using a perfusion model for the real-time determination of membrane-bound acetylcholinesterase activity.

Abstract: The purpose of these experiments was to compare oxime-induced reactivation rate constants of acetylcholinesterase from different human tissue sources inhibited by organophosphorus compounds. To this end, preliminary testing was necessary to generate a stable system both for working with erythrocytes and musculature. We established a dynamically working in vitro model with a fixed enzyme source in a bioreactor that was perfused with acetylthiocholine, Ellman's reagent and any agent of interest (e.g. nerve agents, oximes) and analyzed in a common HPLC flow-through detector. The enzyme reactor was composed of a particle filter (Millex-GS, 0.22 microm) containing a thin layer of membrane-bound acetylcholinesterase and was kept at constant temperature in a water bath. At constant flow the height of absorbance was directly proportional to the enzyme activity. To start with, we applied this system to human red cell membranes and then adapted the system to acetylcholinesterase of muscle tissue. Homogenate (Ultra-Turrax and Potter-Elvehjem homogenizer) of human muscle tissue (intercostal musculature) was applied to the same particle filter and perfused in a slightly modified way, as done with human red cell membranes. We detected no decrease of
acetylcholinesterase activity within 2.5h and we reproducibly determined reactivation rate constants for reactivation with obidoxime (10 microM) or HI 6 (30 microM) of sarin-inhibited human muscle acetylcholinesterase (0.142+/−0.004 min⁻¹ and 0.166+/−0.008 min⁻¹, respectively). The reactivation rate constants of erythrocyte and muscular acetylcholinesterase differed only slightly, highlighting erythrocyte acetylcholinesterase as a proper surrogate marker.

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