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The Effect of Sodium Fluoride on Sarin Inhibited Blood Cholinesterases

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During studies on the mechanism of ageing of phosphorylated cholinesterases some substances were tested for their ability to block ageing of Sarin (methyl-isopropoxy-phosphoryl fluoride) inhibited human plasma cholinesterase. The method used was the one described earlier for *in vitro* reactivation and ageing studies on Tabun inhibited blood cholinesterases.[1] Thus after inhibition at 0°C all samples were dialysed against cold saline for two days in order to remove excess of Sarin. The compound to be tested for its effect upon ageing was added to part of the control and part of the inhibited enzyme immediately before the samples were incubated at pH 7.4 and 37°C. Compounds lowering cholinesterase activity were used in concentrations which gave up to 50 % inhibition of the original enzyme activity.

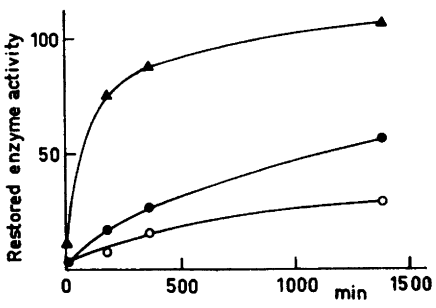

Fig. 1. Return of enzyme activity at pH 7.4, 37°C from methyl-isopropoxy-phosphorylated cholinesterase of human plasma. O = veronal buffer only, ● = veronal bufter and 10^{-4} M sodium fluoride, ▲ = veronal buffer and 10^{-3} M sodium fluoride.

The ability to reactivate the Sarin inhibited enzyme was tested with 10^{-2} M P2S (N-methylpyridinium-2-aldoxime methane sulphonate).

Under the conditions used (veronal buffer) it was observed that 10^{-1} M and 10^{-2} M sodium fluoride prevented ageing; also the compound itself inhibited plasma cholinesterase at this concentrations. Repeated experiments with 10^{-3} M and 10^{-4} M sodium fluoride revealed that the reason for the prevented ageing was to be found in a reversal of cholinesterase activity after addition of sodium fluoride, meaning that these concentrations of sodium fluoride were able to restore enzyme activity before any ageing of the inhibited sample had occurred. As seen in Fig. 1, 10^{-3} M sodium fluoride was able to restore the enzyme activity completely, while 10^{-4} M sodium fluoride only restored part of the activity. Ageing of the still inhibited enzyme was not prevented by 10^{-4} M sodium fluoride. Enzyme activity of a previously aged Sarin inhibited plasma cholinesterase preparation was not restored upon addition of either 10^{-3} M sodium fluoride alone or together with 10^{-2} M P2S.

Experiments also showed that Sarin inhibited human erythrocyte cholinesterase regains enzyme activity upon addition of sodium fluoride. Further experiments are in progress.

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