

53. STRUCTURE AND EFFICIENCY OF CARBAMATES AS DRUGS FOR PROPHYLAXIS

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The usual treatment for organophosphate (OP) poisonings is a combination of atropine and some oximes. This is not effective against poisoning by soman, cyclosarin and tabun on account of rapid dealkylation of acetylcholinesterase (AChE). Previously, it has been shown that pretreatment with certain cholinesterase reversible inhibitors like physostigmine gave appreciable protection against the poisoning by any OP, including soman. In this paper a number of carbamates have been tested for their ability to protect mice, rats, cats and dogs against paraoxon, armine and soman poisoning.

A series of phenyl, naphthyl and pyridyl carbamates with different chains between rings and with different substituents on the rings were tested. In the experiments in vitro the anticholinesterase activity of carbamates and the influence of compounds on phosphorylation of AChE by OP was studied also. There was no correlation between the protective activity of the carbamates and either their chemical structure or toxicity and anticholinesterase activity.

The present study has shown that protective effect of carbamates no doubt depends primarily upon the ability of the carbamate to inhibit the brain AChE with the partial protection of the enzyme against following phosphorylation. Many factors (such as their ability to cross the blood - brain barrier, duration of anticholinesterase action, inhibition of brain AChE reversibly, ability of acetylcholine to increase the speed of gradual decarbamylation of enzyme) are involved in determining of protective efficiency. It has been found that some carbamates with irreversible mode of action increased the toxicity of OP. The efficiency of carbamates also depends on animal species. In mice and rats carbamates gave a weak protection whereas in cats and dogs the protective effect was significantly more. A few most effective carbamates with a longer duration of protective action than physostigmine were study in more detail in conjunction with atropine and as a components of prophylactic antidotes.

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