

The toxicity of pesticides can be reduced by cholinesterase activity

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The main action mechanism of organophosphorus compounds (OP) is the inhibition of acetylcholinesterase (AChE) that causes the accumulation of the neurotransmitter acetylcholine and excessive stimulation of nicotinic and muscarinic receptors in the central and peripheral nervous system, leading to the paralysis of cholinergic synaptic transmission. Related enzyme, butyrylcholinesterase (BChE), is not physiologically essential, but it serves as a backup for AChE and protection of synaptic AChE from man-made and naturally occurring poisons. Both enzymes should be reactivated by strong nucleophiles such as oximes to avoid severe health effects after exposure to OP. However, both inhibition and reactivation are fine-tuning chemical processes that depend on the structure of all reactants. As the interactions of AChE and BChE with ligands and inhibitors are complex, a comprehensive approach involving *in silico*, *in vitro* and *in vivo* research that could lead to the development of new drugs and reactivators AChE and BChE will be presented.



Zrinka Kovarik is permanent research adviser at the IMROH and associate professor of biochemistry and medicinal chemistry at the University of Zagreb, Faculty of Science. She received Ph.D. at the University of Zagreb. For postdoctoral study she was trained at the UCSD, USA. Her research is focused on cholinergic mechanisms and modulation of neurotransmission in poisonings and on cholinesterases - enzymes with key roles in organophosphorus poisoning and in the treatment of neurodegenerative diseases. She is PI of more than 10 research projects, supervisor of 9 PhD thesis, co-author of >100 paper

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