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# SELECTED PESTICIDES AS ACETYLCHOLINE ESTERASE INHIBITORS: THEORETICAL AND EXPERIMENTAL STUDIES

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**Ligand-based or structure-based *in silico* methods, as well as *in vitro* methods were used for the evaluation of the inhibition of *Mus musculus* and *Homo sapiens* acetylcholinesterase by commercially available selected pesticides. Crystal structures of simazine, monocrotophos, dimethoate, and acetamiprid were used for the unconstrained conformational search with various force fields (FFs) implemented in Monte Carlo/Multiple Minimum (MC/MM) approach. Unconstrained conformational searches were applied in the determination of intersynaptic pre-bound conformations of other commonly used pesticides (atrazine, propazine, carbofuran, carbaryl, tebufenozide, imidacloprid, diuron, monuron, and linuron). Moreover, energies of global minima, calculated with the best performing FFs, were compared with selected pesticides toxicities against *Mus musculus*. For the majority of pesticides, low energies of global minima in pre-bound states correlate with high toxicity. The targeted pesticides are acetylcholinesterase (AChE) inhibitors, so structure-based (SB) studies, in the form of molecular docking and molecular dynamics (MD) on either *Mus musculus* AChE (mAChE) or *Homo sapiens* AChE (hAChE), were performed to predict their pharmacology. The mechanistic pathways were established, and additionally confirmed by QM DFT mechanistic studies, which can be further used in the discovery of novel pesticides with desirable lower toxicity against humans. We paid special attention to the mechanism of hAChE inhibition by atrazine, propazine, and simazine. The QM DFT (quantum mechanics – density functional theory) mechanistic studies implied that atrazine, propazine, and simazine could be considered as reversible hAChE inhibitors, administered in high concentrations, and confirmed by concentration-dependent kinetic studies of hAChE inhibition.**

## Biography

Biljana B Arsic pursued her PhD on the investigation of macrolide antibiotics as anti-bacterial and potential anti-malarial medicines at The University of Manchester, United Kingdom. She is a scientific associate in the department of mathematics, faculty of sciences and mathematics, University of Nis, Republic of Serbia. She has published 37 papers in peer-reviewed journals in english, two books in Serbian related to teaching, one chapter in the edited book in english, and attended numerous conferences and symposia. She worked as an associate editor, also was a member of the editorial board, and is currently reviewer for numerous journals in english.

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