Computational Designing and Evaluation of Some Organophosphates and Neonicotinoids Derivatives and Prospects for the Control of Some Insect Pests

A Thesis
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By

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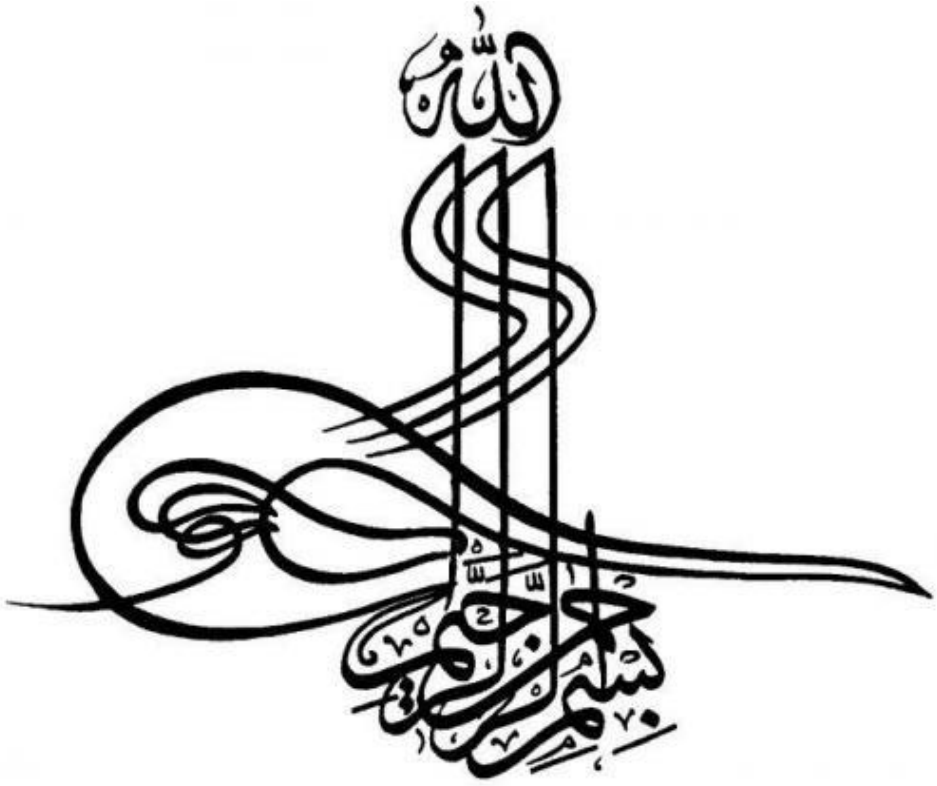
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Abstract

Organophosphates (OPs) and neonicotinoids are widely used for the control of house fly, *Musca domestica* L. (Diptera: Muscidae) as baits and larvicides. This study aimed to design and computational evaluation of novel OP derivatives and imidacloprid (IMI) analogues with high selectivity and insect toxicity based on structure activity relationships (SARs) studies. The conventional OPs and neonicotinoids as well as new structures were docked to their target enzymes for the hypothetical potencies comparison. OP1 was synthesized and the structure was confirmed by ^{1}H NMR, IR and Mass.

OP1 exhibited higher toxicity than chlorpyrifos when assayed by feeding technique to susceptible and field strains of house fly adults and larvae. Comparative docking and toxicological studies of IMI and thiamethoxam (THIA) showed variations between their results that might be due to their metabolic products. The biochemical studies showed reduction in protein content while, ATP-ase, cytochrome P-450 and carboxylesterase activities increased with different levels to tested insecticides treatments. OP1 and chlorpyrifos reduced the AChE activity in contrast to IMI and THIA.

Key words: OPs, neonicotinoids, house fly, molecular docking and SARs.

Abbreviations

^{1}HNMR	Proton nuclear magnetic resonance
2D-QSAR	Two-Dimensional Quantitative Structure-Activity Relationship
3D-QSAR	three-Dimensional Quantitative Structure-Activity Relationship
Ach	Acetylcholine
AChE	Acetylcholinesterase
AChR	Acetylcholine receptor
ATP-ase	Adenosine Triphosphatase enzyme
CarE	Carboxylesterase
ChE	Cholinesterase
***Dm* AChE**	*Drosophila melanogaster* acetylcholinesterase
HRMS	high-resolution mass spectrometry
IMI	Imidacloprid
IR	Infera radiant
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
***Ls*-AChBP**	*Lymnaea stagnalis* acetylcholine binding protein
nAChR	nicotinic acetylcholine receptor
OP1	Newly synthesized organophosphate compound
OPs	Organophosphates
P-450	cytochrome P-450 monooxygenase
QSAR	quantitative Structure-Activity Relationship
R	Resistance
RR	Resistance ratio
S	Susceptible
SAR	structure activity relationship
THIA	Thiamethoxam