

MOLECULAR DOCKING STUDY OF A NOVEL 1,3,4-OXADIAZOLE DERIVATIVE TARGETING INSECT ACETYLCHOLINESTERASE (AChE)

Sh. Kadirova, J. Abdurakhmanov, Sh. Khasanov, A. Ziyaev., Sh. Azimova

S.Y. Yunusov Institute of the Chemistry of Plant Substances, 77, Mirzo-Ulugbek Str.,
Tashkent, 100170, Uzbekistan

The increasing resistance of agricultural pests to conventional insecticides and the growing environmental concerns associated with neonicotinoids have created an urgent need for the development of new insecticidal agents with improved selectivity and lower ecological impact. Heterocyclic compounds containing the 1,3,4-oxadiazole scaffold have attracted considerable attention because of their broad spectrum of biological activities, structural diversity, and favorable physicochemical properties. Among them, sulfur-containing oxadiazole derivatives represent promising candidates for the development of environmentally safer insecticides capable of targeting essential enzymes involved in insect neurotransmission.

A novel 1,3,4-oxadiazole derivative, 2-[(2-chloro-6-fluorobenzyl)sulfanyl]-5-[4-(dimethylamino)phenyl]-1,3,4-oxadiazole, was synthesized by alkylation of the corresponding 5-(4-dimethylaminophenyl)-1,3,4-oxadiazole-2-thione according to the previously developed synthetic procedure. The chemical structure of the obtained compound was confirmed using IR, ^1H and ^{13}C NMR spectroscopy.

The insecticidal potential of the synthesized compound was evaluated *in vitro* using insect cell lines derived from *Helicoverpa zea*, *Trichoplusia ni*, and *Lymantria dispar*. Cell viability was determined by the MTT assay following exposure to the test compound at different concentrations. The investigated derivative demonstrated pronounced inhibitory activity against all three insect cell lines, with biological efficacy approaching that of the commercial insecticide Imidacloprid, indicating its potential as a promising lead compound for agricultural pest control.

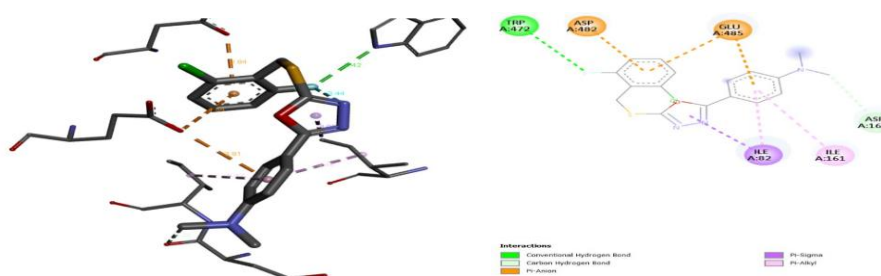


Figure 1. *In silico* analysis of the receptor–ligand interaction between 2-[(2-chloro-6-fluorobenzyl) sulfanyl]-5-[4-(dimethylamino) phenyl]-1,3,4-oxadiazole and acetylcholinesterase (PDB ID: 6XYS).

To investigate the possible molecular mechanism of action, *in silico* molecular docking studies were performed against insect acetylcholinesterase (AChE, PDB ID: 6XYS). Molecular docking analysis revealed that the ligand was stably accommodated within the active site of acetylcholinesterase through interactions with key amino acid residues, including Trp472, Asp482, Glu485, Ile82, Ile161, and Asp160, involving hydrogen bonding as well as π -anion, π -alkyl, and π - σ interactions (fig. 1). The predicted binding pattern supports the experimentally observed insecticidal activity and suggests that inhibition of acetylcholinesterase may represent one of the principal mechanisms underlying the biological effect of this novel 1,3,4-oxadiazole derivative.