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In silico studies on acetylcholine receptor subunit alpha-L1 for proposal of novel insecticides against *Aphis craccivora*

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Overview

- Aphis craccivora is known as one of the most common aphids in the tropics nowadays and has an extended distribution worldwide. This aphid is an important pest especially in groundnuts, cowpeas and numerous other leguminous crops.
- It was observed resistance to organophosphate, nicotine, pyrethroids and organochlorine insecticides in A. craccivora populations on various plant species. Therefore, finding new potential pesticides to prevent the resistance issue is a legitimate goal.
- In this study, for a better understanding of the mechanism of action of neonicotinoid and neonicotinoid-like compounds we conducted an in silico experiment consisting of homology modelling and molecular docking procedures. A small dataset of 648 compounds retrieved from literature based on the similarity with highly potent neonicotinoids was docked in the binding site of the homology model.
- Knowing that neonicotinoids are pesticides involved in the decline of bees the dataset was preliminarily investigated using the BeeTox tool to predict the bee toxicity of these compounds and they were found to be safe.
- The aforementioned dataset was used to explore the intermolecular ligand-target interaction patterns for a rational design of desired insecticides. The docking results were analyzed, by inspecting the key ligands – target interactions and the ranking of the docking scores.

Methods

HOMOLOGY MODELING

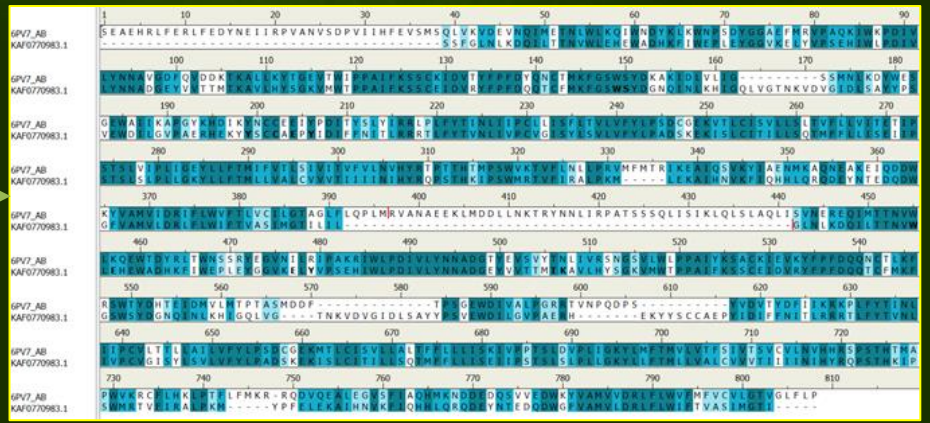
Target

- Acetylcholine receptor subunit alpha-L1 [*A. craccivora*]
- KAF0770983.1 - GenBank ID

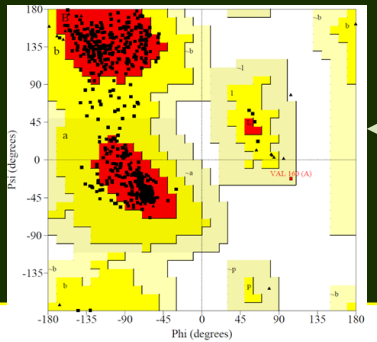
Template

- Fusion protein of Neuronal acetylcholine receptor subunit alpha-3 and Soluble cytochrome b562|Homo sapiens
- 6PV7 – PDB ID

Alignment



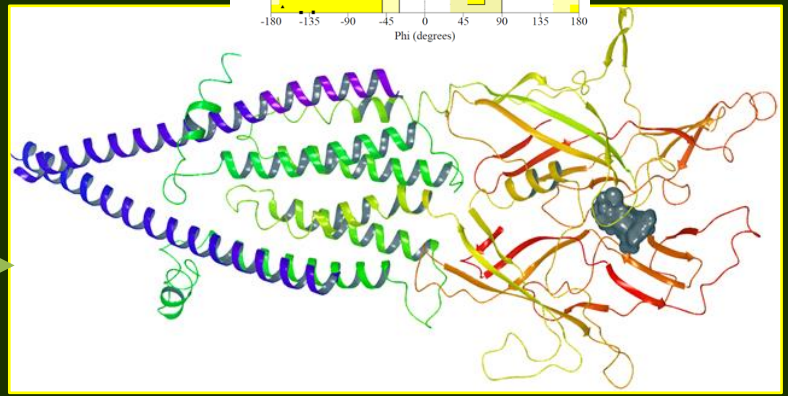
Blast server



The Ramachandran plot: 90.4% residues in most favoured regions

Homology Model

Swiss Model software



Methods

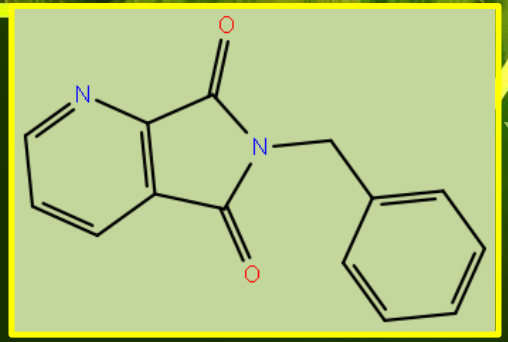
LIGAND PREPARATION

Dataset collection
Literature
(648 compounds)

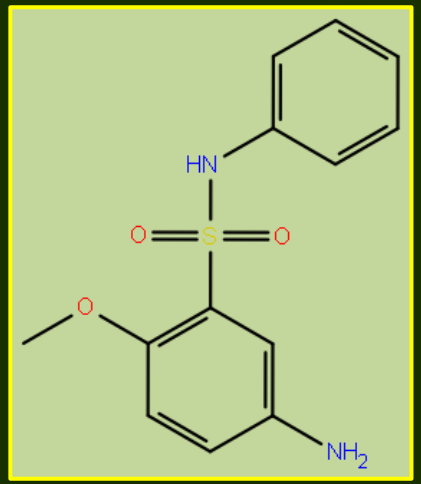
BeeTox tool
(predicted safe for bees)

Omega software
(55 547 conformers generated)

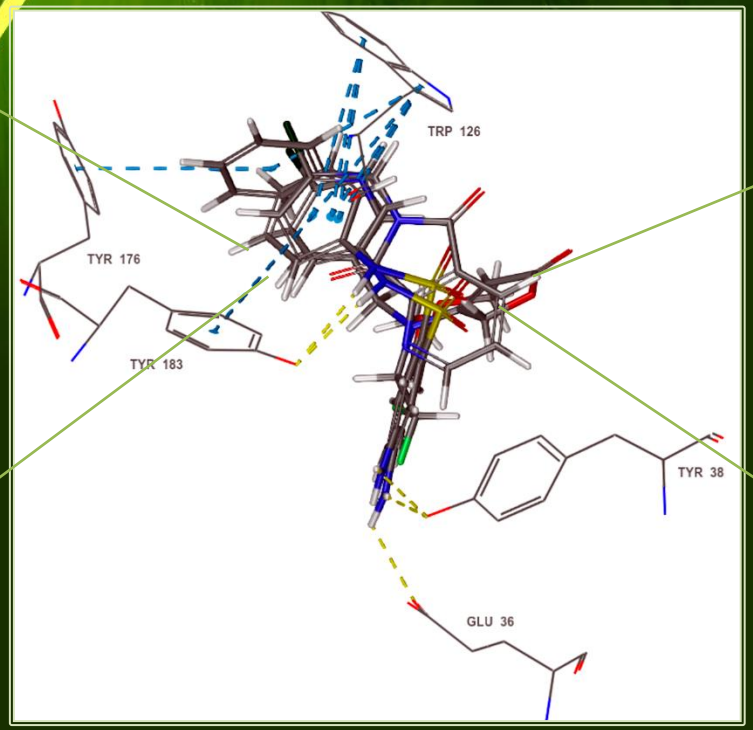
Results and Disscusion



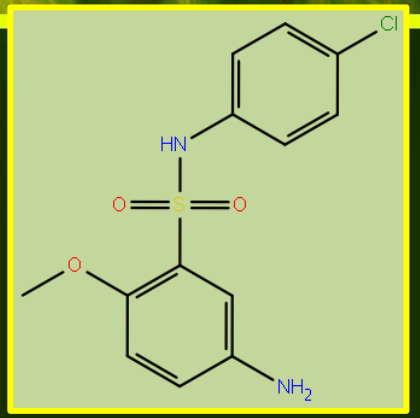
FRED Chemgauss4 score -10.759



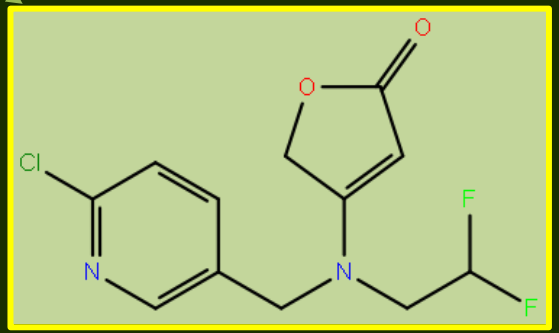
FRED Chemgauss4 score -10.748



The binding site of acetylcholine receptor homology model along with the four top ranked compounds



FRED Chemgauss4 score -10.493



FRED Chemgauss4 score -10.353

Conclusions

- A qualitative homology model for the acetylcholine receptor subunit alpha-L1 of *Aphis craccivora* was built.
- A dataset of structures retrieved from literature was docked in the binding site of the receptor.
- Additionally, the toxic character on bee of these compounds was evaluated with the aid of BeeTox server.
- Four top ranked compounds resulted from docking were proposed.
- Their poses showed important hydrophobic and hydrophilic interactions with the residues, which were, also confirmed by other studies as being key amino acids in the acetylcholine receptor – neonicotinoid insecticide interactions.
- They were predicted to be safe, thus, we can conclude that the compounds proposed by us could be further tested to confirm their potential insecticidal activity against *A. craccivora*.

Acknowledgements

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