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COMPUTATIONAL INSIGHTS INTO NATURAL BIOACTIVE COMPOUNDS INTERACTING WITH MOSQUITO PROTEINS

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ABSTRACT

Mosquito control programs have traditionally relied on synthetic pesticides, which pose significant risks to the environment and non-target organisms. In response to these concerns, naturally derived plant compounds have emerged as promising alternatives due to their eco-friendly and target-specific nature. Recent research has increasingly focused on using protein inhibitor strategies to manage insect pests by targeting their digestive enzymes.This review highlights the potential of using in silico techniques, particularly molecular docking and molecular dynamics simulations, to evaluate the interaction between mosquito gut proteases and naturally occurring protein inhibitors. These computational approaches allow for the prediction and assessment of ligand–protein interactions, facilitating the identification of potent inhibitor candidates. Such analyses can significantly streamline the development of novel biopesticides and transgenic approaches by reducing the cost and time associated with traditional in vitro testing.By providing insights into the structural compatibility and binding affinity of natural compounds with mosquito proteins, in silico methods serve as valuable tools for the sustainable and strategic control of mosquito populations.

INTRODUCTION

The latest test for the control of several insect pests and vectors by insecticide, larvicidal and mosquito repellent has been carried out with natural compounds of plant origin[1]. In the design and development of medicine and insecticide of interest, various bioactive chemicals in plants and computational methods play a key role [2]. Advances in computer technology have allowed virtual screening to influence the process of discovery positively. Virtual screening uses a data set to dock and evaluate each chemical, and the approach employed is based on a prediction of the binding modes and connectivity of each compound by docking an X-ray crystallography [3]. In several insect investigations, various variables, such as ligand size and variety, a wide range of targets and the evaluation of docking programmes, have been examined.

Docking is a computer system which tries to match two molecules best: one receptor and the ligand. In drug design, the main notion is to comprehend the way of selectively restricting the binding in suitable configurations at the active site of the receptor[4]. Modeling homology is used mostly to predict protein structure and creates a model of an amino acid protein resolution sequence. The quality of the homology model depends on the sequence and template structure quality [5].

It is a feasible approach since it generates models that may be utilised for future study, by comparing it with a known template, to predict the 3-D structure of a macromolecule with an unknown structure (target). In giving insight into their molecular function, the three-dimensional (3D) structural features of proteins are important. An additional 3D structural analysis will help to identify binding locations and may result in the design of novel medicines[7].

The growing requirement for a new medication/insecticide leads to the calculation of possible drugs via the drug docking method. The method includes the prediction of ligand shaping and guidance within the targeted site[8].

Computer simulation and molecular screening investigations have become an essential element of many current drug development efforts based on structure. Knowledge of protein and ligand interactions with individual medicines can thus give

an important overview of the drug's binding interactions and relativity[9]. In numerous biological processes such as signal transmission, cell regulations and other macromolecular assemblies, molecular recognitions, including pharmacoprotein interactions play essential roles[10]. Therefore, it is essential in order to comprehend the interaction to determine the binding mechanism and affins between the molecule mechanisms and to design therapeutic interventions [11].

The main proteins that are used to carry odorants and pheromones into the olfactory receptors of insects are considered to be odorant binding proteins[12]. Members of these families of proteins have been discovered and are helping in the search for behaviour[13] in a variety of insect species including Culex quinquefasciatus. Chemicale (Semiochemicals) signals are recognised as including differential attraction of insects towards the hosts as the major function of Odorant Binding Protein (OBP).

The non-specific sterol carrier protein (SCP-2) was initially identified, since cholesterol transporters engaged in cholesterol and intracellular lipid trafficking in spinal cells are also implicated in the cholesterol transportation. It is a low protein of 14 kilogrammes of dalton molecular weight. SCP-2 is part of a family of sterol-binding proteins with a stomatin domain[15]. SCP-2 Vertebrate SCP-2 has an association with various ligands including cholesters, straight chain fatty acid and kinked chain fatty acid [16] and a non-specific lipid carrier protein.

The SCP-2 mosquito seems to constitute a distinct non-peroxisomal and low-weight molecular protein within the SCP-2 family of genes. AeSCP-2 binds to cholesterol and the grains of fatty acids, similar to SCP-2 vertebrates[17]. It appears that AeSCP-2 is an essential gene for mosquitoes to survive and thrive. AeSCP-2 knockdown in mosquito larvae causes significant mortality in emerging adults while AeSCP-1 silence in adults reduces fertility (Fuchs et al., 2001). AeSCP-2 inhibitors are expected to interfere with mosquito larvae's absorption of cholesterol and lead to death[18].

The metabolic intermediate of tryptophane breakdown is 3-hydroxycycynureine, which results in a spectacular oxidative stress response in the mammalian tissues. The excess of this hazardous intermediate metabolic product is rapidly eliminated in the Anopheles gambiae by a particular transaminase, 3 - HK, which is converted in xanthureenic acid to a more stable molecule. Xanthurene acid has a key function in plasmodium gametocyte development and fertility in anopheline mosquitoes that spread malaria. Thus one appealing way of developing malaria transmission that blocks medicines and pesticides seems to interfere with XA metabolism [19]. Pheasant extract phytochemicals may be an alternative technique of determining viable inhibitor compounds which block carriers' proteins to detect novel and more efficient mosquito control agents[20].

CONCLUSION

The integration of advanced computational biology tools has revolutionized the preliminary screening of protein-protein interactions, particularly in the context of mosquito control strategies. In silico methodologies, such as molecular docking and molecular dynamics simulations, enable the identification of potential natural inhibitors targeting mosquito digestive proteases. These approaches not only expedite the discovery process but also reduce the reliance on extensive in vitro testing, thereby conserving resources and time. By leveraging these computational techniques, researchers can efficiently pinpoint promising bioactive compounds, paving the way for the development of eco-friendly and targeted insecticidal agents.

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