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# Computational Screening Approaches for Drug Discovery and Vaccine from Plant Derived Products Against Mosquito-Borne Diseases

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**Abstract:** In order to deal correctly with difficulties, modern technology like computer tools and experimental techniques must be used quickly and efficiently. Ligand-binding sites are frequently the beginning point for protein annotation and drug design structures. In recent decades, several computer approaches have been developed for the prediction of binding sites. Knowledge of the 3D structures of protein has been known for long, but new advancements have altered the possibilities drastically in genome sequencing, robotics and bioinformatics. These high-performance structural determination methods can offer strong screening approaches in recent days.

**Keywords:** Molecular docking, Computational screening, Ligand, Protein

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## Introduction

Genetic and chemical methods are the two primary techniques for mosquito control. In genetics studies, many approaches are developed to change the genetic pathways of mosquitoes, such that illnesses can not be transmitted, but blood meals may still be used (Chesnut *et al*., 2019). Uncertainties concerning the release of genetically modified organisms into the environment are the difficulty with this method. There are therefore more practicable fine-tuned chemical strategy; just one substance that acts for a short time and aims for a single insect is selected (Gopal and Kannabiran, 2003). These compounds should only be insecticides to kill low residue mosquitoes and should not proceed along the same route as DDT (Reegan *et al*., 2016). A promising strategy should be taken towards the blockage of target proteins in the physiology of insect mosquitoes and the creation and discovery of possible inhibitions (Ghaffar *et al*., 2020).

Homology modelling is used mostly for protein structure prediction and develops an atomic resolution model for a series of queries of amino acid proteins (Singh *et al.,* 2017). The quality of the homology model depends on the sequence and template structure. Molecular docking and molecular screening investigations are now fundamental to many current drug development efforts based on structure. Therefore, knowledge of protein and ligand interactions with a particular medication can offer a meaningful understanding of the drug's binding interaction and relativity (Ahmad *et al*., 2015).

In giving an insight into their molecular activities the three-dimensional (3-D) structure of proteins is of great concern. Further 3D structural research will assist identify binding sites and may lead to the development of novel drugs (Singh *et al.,* 2017). Homology modelling is only a feasible approach, since it creates models that can be utilised for further study and it also helps forecast the 3D macromolecule structure with an unknown structure (target) (Youn *et al*., 2014).

Virtual scanning takes into account the data set's docking and scoring of each compound and is based on the prediction of binding modes and binding affinities by connecting to an X-ray-crystallographic structure of each compound in the dataset. In a recent research, some aspects such as the quantity and variety of the ligand data have been examined, and a broad range of targets and assessments have been undertaken (Balachandran *et al*., 2021). In light of the fact that numerous ligands are docked in various directions and may frequently miss co-operations that are known to be significant for the objective receptor, this turns out to be more troublesome as the size of the dataset increments along these lines. Another methodology is to kill inauspicious mixtures prior to docking by limiting the dataset to medicate like mixtures by sifting the dataset dependent on suitable property and sub-underlying highlights and by performing variety examination (Talukdar *et al*., 2017).

Protein-protein docking is a highly computational approach. The quality of the docking techniques shows that we have unlimitedly input domain III of dengue virus serotype I and 4E11, known as heterodimeric crystal structures (Devillers, 2018), in the prediction of Den-Envelope-DC- SIGN and Den-Envelop-2G12 interaction of Z dock, for testing.

*Sterol carrier protein*:

SCP homology, including insects, is observed across the animal kingdom. A number of essential intracultural enzymes are missing in insects, which is why cholesterol food synthesis sources for their steroid derivatives are completely dependent on external sources (Jeneta *et al*., 2019). Thus SCP-2 requires that insects have cholesterol systems that are necessary throughout their life cycle for absorption, transport, and storage. Two key biological requirements must be met by intracellular transport of cholesterol in insects (Liu, 2015).

Two major biological demands must be met for intracellular cholesterol trafficking in insects: first, the need to absorb free cholesterol in cell membrane structure and, later, cholesterol as a precursor for steroid production. These two routes most likely metabolise cholesterol with the same intracellular transportation protein(s). As part of this job, SCP-2 seems to be a good candidate (Taktak *et al*., 2019).

Sterol Carrier Protein or the quasi transmission protein were initially identified because it is a minor protein with a molecular weight of 14 kDa, among cholesterol transporters engaged in cholesterol and lipid in vertebrates intracellular transportation. SCP-2 belongs to the sterol-binding domain and stomatin protein family (Hussein *et al*., 2018). HSD17B4 has a close localising sequence at the C-terminus, which targets these proteins to the peroxiosome, according to SCP-2 SCP-X vertebrates (Scotti *et al*., 2018).

An independent gene identical to SCP-2 has been discovered in the yellow fever mosquito

*Aedes aegypti*. In the midgut of the larvae, and large cholesterol-reliefs (Komala *et al*., 2014). This protein also exhibits a high expression. A distinct non-peroxisomal, low molecular weight protein seen in SCP-2 genes seems to be the mosquito SCP-2 (AeSCP-2). Similar to SCP-2, AeSCP-2 binds similarly to cholesterol and fatty acids, both SCP-2 vertebrate and AeSCP-2 enhance the intake of cholesterol over expressing cells (Dhivya and Manimegalai, 2013).

The insects are not cholesterol-synthesizing; they may become part of the cholesterol shotter and dietary steroids of the lysosomes that are transferred into the endoplasmic reticulum and mitochondria from external sterols into the cell (Adejoro *et al.*, 2016). In an endoplasmic reticulum, SCP-2 may also take part in the conversion of cholesterol to mitochondria for steroid biosynthesis, after conversion of dietary sterols to cholesterol or cholesterol to 7-dehydrocholesterol. The absence of peroxisomal sequence located in the AeSCP-2 C-terminus implies that the cholesterol can be absorbed or trafficked by AeSCP-2 (Adejoro *et al*., 2016).

*D-7 Salivary gland protein*:

Blood-sucking arthropod saliva includes a complex and varied combination of anti-hemostatic, anti-inflammatory, and immunomo-dulation (Vincent *et al*., 2020). D7 salivary protein family is widely expressed in blood-feeding diptera and is distantly associated with the superfamily odorant binding protein. The long and short proteins D7 occur in mosquitoes (Srinivasan *et al*., 2015; Loza-Mejía *et al*., 2018). Specimen lipocalins developed as ticks and kissing bugs acting as effective breastplates of biogenic amines, and the D7 proteins had a similar role. We thus produced a D7 long form from *Aedes aegypti* (Jankowska *et al*., 2018) and five members of the African Malaria Vector family *Anopheles gambiae*.

The D7 family has been found as particularly expressed among several distinct protein families of adult Diptera (Nag and Chowdhury, 2020), which is unique to hematophagous arthropods. These proteins are distant families of the superfamily odorant-bound protein, a separate branch of which they are. Two D7 subfamilies occur in mosquitoes, the short family of 15 to 20 kDa and the large one of 27 to 30 kDa (Thireou *et al*., 2018).

The most common African vector of malaria, *Anopheles gambiae*, contains three long and five short D7 proteins, organised in a reverse tandem with a 3R chromosomal arm (Kumar *et al.,* 2012). One short D7 protein, called hamadarin, is produced and has been found to have anticlotting action in closely related *Anopheles stephensi* mosquito. For other members of the proteins that have 40% amino acid similarity, no further function has been described (Nongonierma and Fitz Gerald, 2017). D7 proteins may act as scavenger of biogenic amines or other haemostasis agonists, such as ticks and kissing bugs with salivary lipocalines (Sharma and Awasthi, 2021).

The lack of an anti-clotting effect of parallel D7 and Hamadarin-related proteins shows that the inhibition of the intrinsic blood coagulation pathway has developed primarily inside the D7r1 hamadarin branch. This branch's terminal location in the evolutionary tree implies that this antimonopoly activity developed exclusively within the anopheline lineage (Sanni *et al*., 2018). In the blood-sucking insect *Rhodnius prolixus* the distinctive feature of the hamadarin homolog is the only anti-pelling protein in other short D7 proteins. The widespread presence of D7 long and short proteins in both culicines and anophelines implies that they played an important role in the early development of mosquito blood feeding (Maia and Amador, 2018).

Histamine associating with D7 molecules may have developed concomitantly or later than the adjusting role of serotonin, since host vertebrates have been 'studied' in the detection of blood sugars with immune mast cell degradation and the release of histamin irritation within 1 min of biting. Although certain mammalian platelets contain as much histamine as serotonin in non-

mammalian thrombocytes, the quantities of histamine are unknown (Thillainayagam *et al*., 2020).

The development of D7 protein NE binding may also be linked to the vascular heats exchange regulation in homeothermal animals (Devillers *et al*., 2014). For example, human epidermis has 10 times as much blood arteries as necessary for metabolism in an organ. Most of these arteries are under normal conditions, closed due to active sympathetic noradrenergic vasoconstriction, but in hyperthermia a decrease in the noradrenergic tonus might cause environmental heat loss (Pervaiz *et al*., 2018). Accordingly, additional adaptation to hematophagia may take place, even if the skin of a cold animal is vasoconstricted, by sequestering NE, when the bloodsucker develops a method to provide the meal. Accordingly, despite aiding mosquitos in feeding blood for more than 120 million years, D7 proteins remain to be functional (Eswaramoorthy *et al*., 2021). Herbal extract phytochemicals might serve as an alternative technique for identifying potential inhibitor compounds that will block carrier proteins and may cause new and more efficient mosquito control agents to be discovered (Prakash *et al.,* 2010).

## Conclusion

The mechanism of chemical action of new biocidal agents has shown significant attention in recent study. A novel approach to rational design may lead to the development of new compounds with potential biocidal activity and to yet, a new insecticide has not been produced that operates directly with regard to inhibition of proteins of mosquito physiology. Initial molecular docking studies enabled us to only identify compounds competing with the protein active region. The results achieved in this context have been regarded satisfactory as they allow the selection of structures with strong pharmacological and toxicological characteristics which are crucial to choose more effective mosquito borne illness compounds.

## References


Adejoro IA, Waheed SO and Adeboye OO. (2016) Molecular docking studies of *Lonchocarpus cyanescens* triterpenoids as inhibitors for malaria. J Phys Chem Biophys. *6*(2): 1000213.

Ahmad A, Javed MR, Rao AQ, Khan MA, Ahad A, Shahid AA and Husnain T. (2015) In-silico determination of insecticidal potential of Vip3Aa-Cry1Ac fusion protein against Lepidopteran targets using molecular docking. Frontiers Plant Sci. 6: 1081.

Balachandran C, Sankarappan A, Chithan K, Natarajan A N, Manickkam J, Elsayed FAA, Abdulaziz AA, Abeer H and Kathirvelu B. (2021) Molecular docking studies of natural alkaloids as acetylcholinesterase (AChE1) inhibitors in *Aedes aegypti*. J Asia-Pacific Entomol. 24(3): 645-652.

Chesnut M, Muñoz LS, Harris G, Freeman D, Gama L, Pardo CA and Pamies D. (2019) In vitro and in silico models to study mosquito-borne flavivirus neuropathogenesis, prevention, and treatment. Frontiers Cell Infection Microbiol. 9: 223.

Devillers J. (2018) 2d and 3d structure–activity modelling of mosquito repellents: A review. SAR QSAR Environ Res. 29(9): 693-723.

Devillers J, Lagneau C, Lattes A, Garrigues JC, Clémenté MM and Yébakima A. (2014) In silico models for predicting vector control chemicals targeting Aedes aegypti. SAR and QSAR Environ Res. 25(10): 805-835.

Dhivya R and Manimegalai K. (2013) Wing shape analysis of the Japanese encephalitis vector *Culex gelidus* (Diptera: Culicidae) at the foot hill of Southern Western Ghats, India. World J Zool. 8(1): 119-125.

Eswaramoorthy R, Hailekiros H, Kedir F and Endale M. (2021) In silico molecular docking, DFT analysis and ADMET studies of carbazole alkaloid and coumarins from roots of *Clausena anisata*: A potent inhibitor for quorum sensing. Adv Applications Bioinformat Chem. 14: 13.

Ghaffar A, Sehgal SA, Fatima R, Batool R, Aimen U, Sliha A, Sajida B, Faheem A and Syed MN. (2020) Molecular docking analyses of CYP450 monooxygenases of *Tribolium castaneum* (Herbst) reveal synergism of quercetin with paraoxon and tetraethyl pyrophosphate: *in vivo and in silico* studies. Toxicol Res. 9(3): 212-221,

Gopal JV and Kannabiran K. (2013) Studies on interaction of insect repellent compounds with odorant binding receptor proteins by in silico molecular docking approach. Interdisciplinary Sci Computational Life Sci. 5(4): 280-285.

Hussein MA, Zyaan OH, Abdel Monsef AH, Rizk SA, Farag SM and Khaled AS. (2018) Synthesis, molecular docking and insecticidal activity evaluation of chromones of date palm pits extract against *Culex pipiens* (Diptera: Culicidae). Int J Mosq Res. 5: 22-32.

Jankowska M, Rogalska J, Wyszkowska J and Stankiewicz M. (2018) Molecular targets for components of essential oils in the insect nervous system--a review. Molecules 23(1): 34.

Jeneta JG, Priya VV and Gayathri R. (2019) Molecular docking of insect-based antimicrobial peptides and their target. Drug Invention Today 11(9): 2254-2257.

Komala S, Ravi S, Usnantaj P, Shanmugam B, Subbaiah GV and Reddy KS. In silico molecular modelling and docking studies on therapeutic target non structural protein 3 (NS3) of dengue virus 1. Int J Pharmaceut Sci Rev Res. 29(1): 37-41.

Kumar PS, Chezhian A, Raja PS and Sathiyapriya JS. (2012) Computational selections of terpenes present in the plant *Calotropis gigantea* as mosquito larvicide's by blocking the sterol carrying protein, AeSCP-2. Bangladesh J Pharmacol. 7(1): 1-5.

Liu, N. (2015) Insecticide resistance in mosquitoes: impact, mechanisms, and research directions. Annual Rev Entomol. 60: 537-559.

Loza-Mejía MA, Salazar JR and Sánchez-Tejeda JF. (2018) In silico studies on compounds derived from calceolaria: phenylethanoid glycosides as potential multitarget inhibitors for the development of pesticides. Biomolecules 8(4): 121.

Maia RT and Amador VC. (2018) Molecular docking for detoxifying enzyme studies. Molecular Docking. doi:10.5772/intechopen.73920.

Nag A and Chowdhury RR. (2020) Piperine, an alkaloid of black pepper seeds can effectively inhibit the antiviral enzymes of Dengue and Ebola viruses, an in silico molecular docking study. Virus Disease 31(3): 308-315.

Nongonierma AB and FitzGerald RJ. (2017) Unlocking the biological potential of proteins from edible insects through enzymatic hydrolysis: A review. Innov Food Sci Emerging Technol. 43: 239-252.

Pervaiz R, Khan MA, Ahmed N, Naeem H and Zafar AU. (2018) Determination of mosquito larvicidal potential of *Bacillus thuringiensis* Cry11Ba fusion protein through molecular docking. Biologia 73(10): 1015-1023.

Reegan AD, Stalin A, Paulraj MG, Balakrishna K, Ignacimuthu S and Al-Dhabi NA. (2016) In silico molecular docking of niloticin with acetylcholine-sterase 1 (AChE1) of *Aedes aegypti* L. (Diptera: Culicidae): a promising molecular target. Med Chem Res. 25(7): 1411-1419.

Sanni DM, Lawal OT and Salawu SO. (2018) In silico phylogenetics and molecular docking studies of rhodanese from yeast (Saccharomyces cerevisiae). J Adv Biol Biotechnol. 17(4): 1-10.

Scotti L, Scotti MT, Yarla NS, Monteiro AF, de Oliveira Viana J, Dantzger DRC and Ishiki HM. (2018) Dengue virus inhibition targets: a review and docking study. Curr Topics Med Chem. 18(18): 1522-1530.

Sharma P and Awasthi P. (2021) Synthesis, Characterization, In vivo, Molecular Docking, ADMET and homo-lumo study of juvenile hormone analogues having sulfonamide feature as an insect growth regulators. J Molec Struct. 1231: 129945.

Singh KD, Labala RK, Devi TB, Singh NI, Chanu HD, Sougrakpam S, Nameirakpam BS, Sahoo D and Rajashekar Y. (2017) Biochemical efficacy, molecular docking and inhibitory effect of 2, 3-dimethylmaleic anhydride on insect acetylcholinesterase. Sci Rep. 7(1): 12483.

Srinivasan R, Natarajan D, Shivakumar MS, Vinuchakkaravarthy T and Velmurugan D. (2015) Bioassay guided isolation of mosquito larvicidal compound from acetone leaf extract of *Elaeagnus indica* Servett Bull and its in-silico study. Indust Crops Products 76: 394-401.

Taktak NE and Badawy ME. (2019) Potential of hydrocarbon and oxygenated monoterpenes against Culex pipiens larvae: Toxicity, biochemical, pharmacophore modeling and molecular docking studies. Pesticide Biochem Physiol. 158: 156-165.

Talukdar P, Mandal S and Ganguly D. (2017) Development of bio-larvicide for *Anopheles stephensi* through selected phytoligands from the leaf of *Eucalyptus grandis* against mosquito acetylcholinesterase: An in silico approach. Int J Adv Res Computer Sci. 8(5): 1078-1088.

Thillainayagam M, Ramaiah S and Anbarasu A. (2020) Molecular docking and dynamics studies on novel benzene sulfonamide substituted pyrazole-pyrazoline analogues as potent inhibitors of *Plasmodium falciparum* Histo aspartic protease. J Biomolec Struct Dynam. 38(11): 3235-3245.

Thireou T, Kythreoti G, Tsitsanou KE, Koussis K, Drakou CE, Kinnersley J, Kröber T, Guerin PM, Zhou JJ, Iatrou K, Eliopoulos E and Zographos SE. (2018) Identification of novel bioinspired synthetic mosquito repellents by combined ligand-based screening and OBP-structure-based molecular docking. Insect Biochem Mol Biol. 98: 48-61.

Vincent S, Arokiyaraj S, Saravanan M and Dhanraj M.

(2020) Molecular docking studies on the anti-viral effects of compounds from Kabasura Kudineer on SARS-CoV-2 3CLpro. Frontiers Molec Biosci. 7: 434.

Youn K, Yun EY, Lee J, Kim JY, Hwang JS, Jeong WS and Jun M. (2014) Oleic acid and linoleic acid from *Tenebrio molitor* larvae inhibit BACE1 activity in vitro: molecular docking studies. J Med Food 17(2): 284-289.