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Research Article

Designing Hypothesis of Quinoline Sulphonamide Hybrid as an Antimalarial Schizonticidal Blood Active Agent: Molecular Docking Approach

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A B S T R A C T

Malaria is deadly parasitic disease and approx 91% region of African countries are at risk of parasitic disease which lead to the 435000 deaths worldwide due to malaria. inspite of having several drugs for the treatment but the disease remains untreated due to the resistance caused in Plasmodium falciparum. Quinoline sulphonamide hybrid is a new approach to eradicate resistance. In the given study molecular docking study was performed using 30 quinoline sulphonamide hybrid analogues PDB code [4 RAN] Aza-acyclic nucleoside phosphonates. On the basis of moldock score molecular docking results revealed that compound number 9 is most active compound to the active site of protein with amino acid Gly169, Lys165, Val187. Docking studies of the compounds was done with the help of Molegro Virtual Docker software using docking method to study their activity.

Keywords: Parasitic, Docking, Hybrid, Quinoline Sulphonamide

Introduction

Malaria remains one of the most widespread challenging infectious diseases especially in the developing countries like India[1]. Malaria is a global infectious disease that remains a leading cause of morbidity and mortality in the developing world. Severe and fatal malaria is predominantly caused by Plasmodium falciparum.[2] Malaria is a serious, mosquito borne life-threatening blood disease.[3] It is generally transmitted through the bite of an infected anopheles mosquito called "malaria vector", which bite mainly during dusk and dawn.[4] Infected mosquitoes carry the Plasmodium parasite.[5] There are 5 parasitic species that cause malaria in humans:[6-8]

- P.vivax
- P.ovale
- P.falciparum
- P.malariae
- P.knowlesi

And amongst them these 2 species - P. falciparum and P. vivax are the most severe and fatal ones.

Modes of Transmission

Malaria does not transmit from one person to another without a mosquito except transmission from[9-10]

- Infected mother to fetus (congenital malaria),
- by transfusion of blood or
- by sharing of needles by intravenous drug users.

Material and Method

The Quinoline Sulphonamide analogues were docked against PDB ID: 4RAN. The steps involved are as follows:

- Ligand preparation

- Protein preparation
- Cavity detection
- Docking

All structures were designed with ChemDrawUltra v8.0 (Cambridge Soft Corporation, Cambridge, MA, USA; http://www.cambridgesoft.com), their 3D structures were draw with Chem 3DUltra8.0 and were further minimized with the Chem 3DUltra8.0, using the MM2 and MOPAC to generate low energy 3-D structure for each input structure and the rest of the parameter values by default. Protein was selected and downloaded from Protein Data Bank (PDB ID: 4RAN) Aza-acyclic nucleoside phosphonates. Dockinganalysis was performed on 30 quinoline sulphonamide hybrid analogues. Molecular docking of quinoline sulphonamide hybrid analogues was done on molegro virtual docker (version 6.0).

Protein was selected and downloaded from RCSB Protein Data Bank (www.wwpdb.org). The protein was imported, optimized and minimized. All the other chains and water molecule were preserved for molecular docking simulations. Designed compounds were subjected to docking analysis for the interaction with protein in order to screen best docked compounds for synthesis.

Before starting the docking run, all potential binding sites (active sites) was identified using the Detect Cavities dialog box. The cavity was selected on the basis of interaction of reported ligand.

The bonds, bond orders, hybridizations, charges and hydrogen atoms were assigned and parameters of docking were optimized which are as follows:

Table 1.Docking Parameters

Number of cavities	03
Grid resolution	2.1Å
Number of runs	10
Probe size	1.3Å
Maximum iteration	21750

After the completion of docking run poses were analysed in the pose organiser view and best pose was selected on the basis of docking score and visual inspection of the interactions between compound and amino acid residues of protein.

Result and Discussion

Docking scores gives an idea about the energyrequired to cover the entire protein by a ligand molecule. On the basis of moldock score molecular docking results revealed that compound number 9 is most active compound to the active site of protein with amino acid Gly169, Lys165, Val187. The Moldock Score of QS-9 was found to be -113.98.

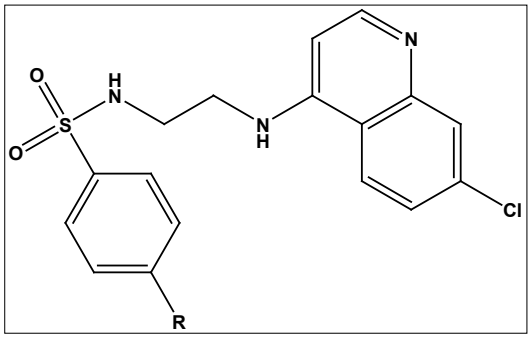
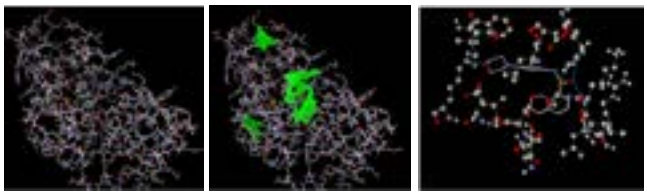


Figure 1.Common structure of Quinoline Sulphonamide



(a) (b) (c)

Figure 2.(a) Protein structure (b) Cavity detection (c) Interaction

Table 2.Moldock Score

S.No.	Compound Number	Moldock score	Rerank score
1	QS-9	-113.98	-91.84
2	QS-5	-106.20	-71.78

Table 3.Hydrogen bond Interaction

S.No.	Ligand compound	Hydrogen bond interaction
1	3L6	Gly169, Asp137, Lys165, Phe186, Val187,
2	QS-9	Gly169, Lys165, Val187

Conclusion

Above study revealed that QS-9 can be used further for in-vitro and in-vivo studies. Selected quinoline sulphonamide hybrid analogues can be studied for their further therapeutic potential as an Antimalarial Schizonticidal Blood Active Agent.

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