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MOLECULAR DOCKING, DRUG-LIKENESS AND SWISSADME EVALUATIONS OF THE INTERACTIONS OF 2'-SUBSTITUTED TRICLOSAN DERIVATIVES WITH *Plasmodium falciparum* ENOYL-ACYL CARRIER PROTEIN REDUCTASE

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ABSTRACT

The orthodox process of investigating lead molecules is a lengthy and laborious one that in most cases leads to minimal success. Molecular docking analysis provides an alternative path to drug discovery through the interactions of two or more complexes. Molecular docking studies were performed on 12 theoretically designed derivatives of 2'-substituted triclosan against a Plasmodium falciparum (P. falciparum) enoyl-acyl carrier protein reductase (PfENR) protein target as well as predicting their drug-likeness and SwissADME properties. The docking studies were carried out using the Molegro Virtual Docker (MVD) where the molecular interactions between the ligands and the target protein were studied. The docking analysis revealed 5-(((5-chloro-2-(4-chloro-2-hydroxyphenoxy)benzyl)amino)methyl) benzofuran-6-ol (re-rank docking score = -145.497 kcal/mol) as the most stable derivative. The compounds were all found to completely concord with the Lipinski rule regulations, in addition to the molar refractivity as well as the number of rotatable bonds appearing within acceptable limits. All compounds except 2–5 and 7 show high gastrointestinal absorption, and are non-inhibitors of cytochrome P450; CYP1A2 and CYP2C19 except CYP2C9, lack BBB penetration, and only compounds 2–7 and 12 were found to inhibit permeability-glycoprotein (P-gp) substrate. The findings suggest that some of the derivatives tend to increase the oral bioavailability of the substrate and most of them cannot be used in the treatment of cerebral malaria. These results may lead to future optimisation of the designed derivatives for improved antimalarial agents.

***Keywords*:** Molecular docking, Drug-likeness, ADME, 2'-substituted triclosan, *Pf-ENR* protein.

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