



Back

Molecular Docking and ADME Profiles of Hyrtiosulawesine Derivatives Targeting pfLDH: Exploring Potential as Antimalarial Agents

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Abstract

The relentless rise in Plasmodium falciparum's resistance to existing antimalarial drugs has sparked an urgent quest for novel therapeutic agents. For centuries, natural resources have been the bedrock of medicinal remedies, with β -carboline emerging as a beacon of hope in antimalarial research. In this study, we delve into the potential of hyrtiosulawesine derivatives as revolutionary antimalarial compounds, utilizing hyrtiosulawesine as the crucial scaffold. Employing a sophisticated amalgamation of molecular docking and ADME (absorption, distribution, metabolism and excretion) profiling, we meticulously screened an extensive library of hyrtiosulawesine's derivatives against P. falciparum. Based on advanced computational techniques, the binding affinities and interaction profiles were assessed and culminating in the selection of the most promising candidates based on their exceptional binding interactions. Moreover, the comprehensive ADME analyses were performed to assess the pharmacokinetic properties of these derivatives, ensuring their suitability as drug candidates. The results showed that most of the analogues exhibited strong binding affinities (-7.2 to -9.8 kcal/mol) to the Plasmodium falciparum lactate dehydrogenase (pfLDH) protein, surpassing that of hyrtiosulawesine itself. Among these, compounds 2t and 1w demonstrated the strongest binding, likely due to hydrogen bonding with Arg171 and Asn197. ADME profiling revealed that all hyrtiosulawesine derivatives displayed favourable drug-likeness properties and adhered to the Lipinski Rule of 5 (Ro5) indicating their potential efficacy as antimalarial agents. This investigation provides a foundation for further in vitro and in vivo investigations paving the way for the development of effective treatments against malaria. © 2024 Asian Publication Corporation. All rights reserved.

Author keywords

ADME; Antimalarial; Hyrtiosulawesine analogues; Molecular docking

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