

al Evaluation And Mechanistic Studies Of Totarol Amino Alcohol Derivatives As Potential Antimalarial Agents.

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URI:

Abstract:

Herein we report on the semisynthesis and biological evaluation of β -amino alcohol derivatives of the natural product totarol and other simple aromatic systems. All β -amino alcohol derivatives of totarol exhibited higher antiplasmodial activity than totarol [IC₅₀: 11.69 μ M (K1, chloroquine and multi-drug resistant strain), and 11.78 μ M (D10, chloroquine sensitive strain)] δ 12e was the most active [IC₅₀: 0.63 μ M (K1), and 0.61 μ M (D10)]. The phenyl and naphthyl β -amino alcohol derivatives were much less active than their corresponding totarol equivalents. The majority of the β -amino alcohol derivatives of totarol were more active against K1 than the D10 strains of *Plasmodium falciparum*, a trend similar to the inverse relationship observed with the established aryl-amino alcohol antimalarial mefloquine. Selected compounds were shown to affect erythrocyte morphology, inhibit erythrocyte invasion and trigger CQ accumulation.