

Screening and Evaluation of Novel Compounds for Antimalarial Activity Against *Plasmodium falciparum*

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Malaria is an infectious disease caused by protozoan parasites of the genus *Plasmodium*. The efficacy of current antimalarial treatments is limited, mainly due to the emergence of drug-resistant parasites. Therefore, the discovery of new antimalarial compounds and the investigation of resistance mechanisms are essential for the development of more effective therapies. This project aimed to screen compounds against *P. falciparum* to identify promising candidates for the development of new antimalarial therapies. The inhibitory activity of the compounds was evaluated against the *P. falciparum* strains 3D7 and Dd2 by determining the IC₅₀ at 72 h. A cytotoxicity assay in HEK293T cells was performed to establish non-toxic concentrations. The antimalarial activity of 16 triazole compounds was evaluated against the 3D7 strain, revealing variation in potency, with FTNBR and FTBB showing the highest activity, while FTBAC, FAN, FTBME, and FAT displayed activity in the micromolar range. These compounds were subsequently tested against the chloroquine-resistant strain (Dd2), in which FTBME and FAN maintained similar activity, FTNBR, FTBAC, and FAT showed increased IC₅₀ values, and FTBB exhibited greater activity. In the cytotoxicity assays, the compounds demonstrated low toxicity at the tested concentrations. The antimalarial activity of other classes of compounds was also evaluated against the 3D7 strain. The tested compounds included indoles (LAM1, LAM2, LAM8, LAM11, LAM12, LAM13, and LAM14), amino acid-derived compounds (LAM3, LAM4, LAM5, and LAM6), an isoniazid derivative (LAM7), a hydrazone (LAM9), and a thiophenol dimer (LAM10). Among the evaluated compounds, LAM10 and LAM14 exhibited the highest antiplasmodial activity, followed by LAM9 and LAM1, whereas LAM11 and LAM12 showed lower potency. These results indicate distinct activity profiles among the compound classes, enabling the identification of promising candidates for further investigation.