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ORIGINAL ARTICLE

Design, Syntheses and Biological Evaluation of 4-Aminoquinoline-Thiazolidinone Hybrids

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Abstract

Over several decades following the introduction of Artesunate, no new anti-malaria drug has been developed. The emergence of resistance towards the existing chemotherapy further necessitates the discovery of novel and more effective drug molecules. The study employs the strategies of molecular hybridization, chemosensitizer and poly-pharmacology to design, synthesize and screen some novel 4-aminoquinoline-thiazolidin-4-one hybrid compounds 3(a-m) as anti-malarial agents. From a total of six hundred designed molecules, the compounds selected through molecular docking were successfully synthesized, and characterized using physical and spectral techniques. They were evaluated for antimalarial activity using *in-vitro* and suitable *in-vivo* model. The compounds exhibited good to moderate activity for *in-vitro* enzyme inhibition potential, with IC_{50} values in the range of 1.81–4.03 µg/mL. Also, the *in-vivo* blood schizonticidal study suggested the compounds to be potent, with percentage parasitaemia inhibition in the range of 70% to 83%, and extended mean survival time up to 27 days. The compounds were also subjected to *in-silico* prediction study. The results obtained from the studies on the series were found to be in sync, establishing 4-thiazolidinone-aminoquinoline as a privileged scaffold for effective and safe anti-malarial agents, and the synthesized compounds as promising anti-malarial agents.

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