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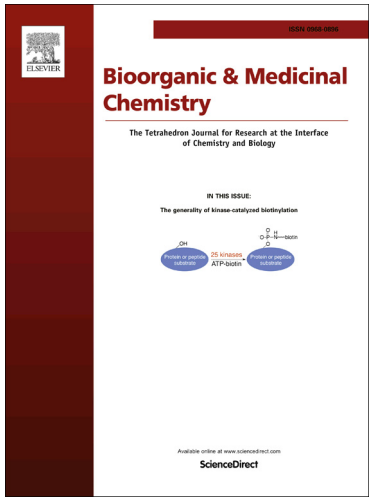

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Synthesis and evaluation of Naphthyl bearing 1,2,3-Triazole analogs as Antiplasmodial agents, Cytotoxicity and Docking Studies

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Abstract

Novel series of naphthyl bearing 1,2,3-triazoles (**4a-t**) were synthesized and evaluated for their in vitro antiplasmodial activity against pyrimethamine (Pyr)-sensitive and resistant strains of Plasmodium falciparum. The synthesized compounds were assessed for their cytotoxicity employing human embryonic kidney cell line (HEK-293), and none of them was found to be toxic. Among them **4j**, **4k**, **4l**, **4m**, **4n**, **4t** exhibited significant antiplasmodial activity in both strains, of which compounds **4m**, **4n** and **4t** (~3.0 fold) displayed superior activity to Pyr against resistant strain. Pyr and selected compounds (**4n**, **4p** and **4t**) that repressed parasite development also inhibited PfDHFR activity of the soluble parasite extract, suggesting that anti-parasitic activity of these compounds is a result of inhibition of the parasite DHFR. In silico studies suggest that activity of these compounds might be enhanced due to π-π stacking.

Keywords

Naphthyl 1,2,3-triazoles; Click chemistry; Antiplasmodial activity; Cytotoxicity; Induced fit docking(IFD)