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Hydroxyethylamine analogs as plasmepsin inhibitors targeting multiple life stages of the malaria parasite

Snigdha Singh and Ramesh Chandra

Department of Chemistry, University of Delhi, India

Abstract

Malaria is a potentially fatal disease caused by genus Plasmodium parasites and Plasmodium strain resistance to existing antimalarial drug made the current approach inadequate for treatment of malaria. New, effective and inexpensive antimalarials against multiple life stages of the parasite are urgently needed to combat the spread of malaria. Elimination efforts require new drug classes that alleviate symptoms, prevent transmission and provide a radical cure. To achieve this goal it is crucial to develop compounds that will exhibit multistage activity preferably with novel and multiple modes of action. However, the renewed malaria eradication guidelines recommended the discovery of new drugs, which can target liver, asexual, and sexual blood stages (that is, multistage activity). Bearing in mind these facts, we decided to build a library of new compounds of chemical diversity based on synergistic association of high-valued heterocycles with phthalimide and hydroxyethylamine scaffolds. Our studies suggested a few potential molecules that exhibited noteworthy growth inhibition of Plasmodium falciparum in culture and P. berghei infection in mouse model with nominal cytotoxicity. Few hits were evaluated as notable multistage growth inhibitors (liver, asexual blood and gametocyte stages) of the parasite in low micromolar inhibitory concentrations. Added experiments presented synergistic interactions with chloroquine and dihydroartemisinin in culture and P. berghei infected mice model. The interesting observations will be presented.

Biography

Snigdha Singh is a PhD Student in Drug Discovery & Development Laboratory, department of Chemistry at University of Delhi, India.

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