Fast tracking antimalarial drug discovery through molecular modelling and repositioning: Lead optimisation of synthetic emetine analogues SALF01/02

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Abstract

Malaria is a life threatening infectious disease caused by a parasitic protozoan belonging to the genus *Plasmodium*. With resistance reported in all categories of anti-malarial drugs, the need for a new class of affordable anti-malarial is an urgent priority. The anti-amoebic drug Emetine dihydrochloride has been identified as a potent antimalarial option (Matthews *et al.*, 2013). Wong et al., reported the target binding site of emetine on 40s subunit of the 80s ribosome.

Two synthetic analogues of emetine SALF1 and SALF2 are modelled on the 40S small subunit of 80S Ribosome. Lead optimisation of SALF1 and SALF2 was done to identify parasite reduction rate and stage specificity. The project includes virtual screening of FDA approved library of drugs against the ribosomal binding site of emetine to fast-track drug discovery. The results have identified synergies between SALF1 and two FDA approved drugs. The proposed anti-malarial combination therapies for synthetic analogues of emetine would potentially reduce the side-effects whilst maintaining the efficacy of the treatment.

Keywords

Molecular modelling, ligand-receptor docking, virtual screening, drug discovery, malaria combination therapy