Virtual screening of antiplasmodial natural products using CADD against pfDHODH

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Abstract

Malaria is a global health concern with the highest morbidities being reported in sub-Saharan Africa. It is a public health concern given the rise of antimalarial drug resistance in the plasmodium parasite whereby *P. falciparum* which causes the most severe malaria has shown resistance to nearly all antimalarial drugs.

This calls for the development of new antimalarial drugs; however, the traditional random synthesis/isolation and screening method of drug discovery is a slow and expensive process hence the need for design of drugs that have a high probability of success. Computer aided drug design (CADD) employs computing power to express molecular properties thus allowing a sizeable amount of molecules to be virtually screened at a go. In this research project, OpenEye CADD software suite was used in docking and shape matching techniques in order to screen a total of 360 antiplasmodial natural products against *Plasmodium falciparum* dihydroorotate dehydrogenase (pfDHODH) for the establishment of a potential lead antiplasmodial compound. pfDHODH is an enzyme that plays a key role in the de novo biochemical synthesis of DNA making it an attractive antimalarial drug target.

The results of this study show that *1,6-dihydroxy-7-methyl-3,10-dioxo-anthracen-9-olate* (Demethylmacrosporine) an anthraquinone isolated from *Rumex obtusifolius* (Polygonaceae) is a potential lead compound for antimalarial drug development targeting pfDHODH . The results

also show the most favourable pose that should be assumed by the compound for effective inhibition of the enzyme.