

## ABSTRACT

Despite the efforts to 'roll back malaria', statistics still shows that there are 97 countries and territories with ongoing malaria transmission, and 7 countries in the prevention or reintroduction phase, making a total of 104 countries and territories in which malaria is presently considered endemic 4. Globally, an estimated 3.4 billion people are at risk of malaria. WHO estimates that 207 million cases of malaria occurred globally in 2012 and 627 000 deaths were registered. Of the cases (80%) and deaths (90%) occurred in Africa. The multi - drug resistance to the widely recommended and provided drug treatments (Chloroquine and Sulphadoxine - Pyrimethamine) across Asia , South America and Africa has prompted the use of Artemisinin - based combination treatments (ACTS) 1. This necessitates profiling of new antimalarial drugs that have low resistant strains towards *P. falciparum*. Strategic plans need to be put in place to discover and develop novel antimalarial compounds that are not encumbered by pre - existing mechanisms of drug resistance to avoid ever - increasing toll of malaria on tropical areas 2 In this research, a computational approach is employed to identify suitable scaffolds from a database of natural products of Kenya ([mitishamba.uonbi.ac.ke](http://mitishamba.uonbi.ac.ke)) that can be used as alternative antimalarial drugs. Benzoxazine (Cappamensin A based on its similarity to Primaquine), Chromones (Abyssinone V, a promising compound) and Naphthoquinone (Lapachol) have been carefully chosen; with IC<sub>50</sub> values of the isolated natural products serving as guiding values. Heavy computational techniques such as Generation of 3 - D molecular database, Virtual Screening, Calculation of probability assignment curves 3, 2 - D and 3 - D similarity searches have been used to identify the natural products of prime focus. Compounds exhibiting high probability of being active based on the calculations have been synthesized and subjected to in vitro assay against PfD HODH enzyme