Mortality of A. gambiae egg stage exposed to lambdacyhalothrin

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Background: Research studies revealed that lambdacyhalothrin (pyrethroid insecticide) – treated curtains, mats and blankets reduced greatly mosquito bites and consequently malaria infection in a small community outside Enugu, Nigeria. The high rate of malaria infection (68.3%) found among children of this area is similar to that in other parts of the country. To some extent it reflects living conditions in the rural areas, for villages have thick vegetation, inadequate drainage systems, house positions and house designs and the climate encourages the breeding of Anopheles mosquitoes. With Lambdacyhalothrin – treated materials, the rate of malaria infection was reduced from 68.3% to 30.25%. However less attention was paid to the actual effect of the insecticide on mosquitoes. This paper presents a study on the toxicity of the insecticide lambdacyhalothrin on the egg stage of Anopheles gambiae – a common malaria vector in Africa.

Methods & Materials: The study was carried out at National Arbo-virus and Vector Research Center, Enugu according to World Health Organization bioassay. Six different concentrations of lambdacyhalothrin (0.001 mg/l, 0.005 mg/l, 0.010 mg/l, 0.015 mg/l, 0/l 0.020 mg and 0.025 mg/l) were prepared from stock solution and used for the study. 650 of egg stage of Anopheles gambiae were selected from insectary bred strain and used for the study. Experimental eggs were transferred into 6 small plastic bowels each containing 200 ml of each of the concentrations. The control was put in the 7th bowl containing 100 ml de-chlorinated water. Eggs mortality was monitored after 24, 48, 72 hours and 7days exposure and data recorded. Data were analyzed using probit analysis and multiple regressions

Results: Percentage mortality of eggs was 7%, 29, 63 and 81% in 0.010, 0.015, 0.020 and 0.025 mg/l respectively after 48 hours test period. LC50 was 0.018 mg/l while LC90 was 0.029 mg/l (Table 2). The implications of these data in mosquito control are discussed.

Conclusion: Lambdacyhalothrin has shown to be a powerful and reliable anti-mosquito agent with low cost, easy to administer and risk free properties. We advocate it for global mosquito/malaria control.

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Antimalarial drug development from phytomedicine: Chemoinformatic and pharmacological studies

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Background: Identification of new compounds, preferably with novel mechanism of actions (MOA), is highly desirable to circumvent resistance of Plasmodium falciparum to current antimalarial drugs. Although large numbers of phytochemicals have shown good in-vitro antiplasmodial activities but hardly any have made it through the antimalarial drug development pipeline. Chemoinformatic and pharmacological characterization of these phytochemicals may be able to identify those with possible unique MOA and desirable pharmacological profile, which is essential for in-vivo/clinical evaluation, hence aid antimalarial drug development. Our research questions included: How similar/diverse are these phytochemicals from current antimalarial drugs? Do these phytochemicals have desirable DMPK (Drug Metabolism and Pharmacokinetics) profiles? What are their binding affinities and mode to drug targets in P.falciparum?

Methods & Materials: Chemoinformatic characterization done include: molecular structure and pharmacophore similarities (Tanimoto coefficient) between these phytochemicals and current antimalarial drugs as well as scaffold analysis to identify unique substructures. Similarity matrices were constructed and data visualized as cluster trees and heat maps. For pharmacological characterization, Molecular Operating Environment, Discovery studio and SMARTcyp software were used to compute molecular features that define DMPK profile and to simulate the binding of these phytochemicals to drug targets in P.falciparum.

Results: The results show that the majority of these phytochemicals (93%) have substructural features that are diverse from current antimalarial drugs but similar pharmacophore features. Unique chemical scaffolds were identified and up to 64% possess desirable DMPK profiles. Molecular docking simulations showed that these phytochemicals interact with important amino acid residues within drug targets in P.falciparum.

Conclusion: The pharmacophore features, unique scaffolds and the highly diversified chemical space of these phytochemicals from current antimalarial drugs gives them the potential to interact with novel drug targets in P.falciparum hence may possess a unique MOA. A good number of these phytochemicals showed good DMPK profiles that may be favourable for them to be moved into clinical evaluation. Molecular docking of these phytochemicals showed important interaction with viable drug targets in P.falciparum and suggest possible MOA. Overall, the data generated for each phytochemicals may allow rational selection of phytochemicals that may be successfully moved through the antimalarial drug development pipeline.

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