

Plan Overview

A Data Management Plan created using DMPTool

Title: Desenvolvimento e análise de toxicidade de derivado do indol com atividade larvicida frente ao *Aedes aegypti* Linn: controle da dengue, chikungunya e Zika.

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Funder: Digital Curation Centre (dcc.ac.uk)

Template: Digital Curation Centre

Project abstract:

The reintroduction of the mosquito *Aedes aegypti* Linn. in Brazil in the 80's started a period of dissemination of diseases transmitted by this mosquito. Upon every new serotype or disease introduced in this country, new epidemics arise. Recently, two new diseases transmitted by this mosquito were introduced in Brazil, namely chikungunya and Zika. Especially, Zika has alarmed health authorities worldwide due to its sexually-transmitting capabilities, microcephaly in newly born babies, and the Guillain-Barré syndrome. These data show that there is an urge to deepen the research not only for treating these diseases, but also to control its mosquito vector. Considering the resistance that the larvae of *A. aegypti* have developed to the larvicides currently used, the development of studies aimed at obtaining effective compounds against the larvae of this mosquito vector are of fundamental importance for human society. In this context, our research group synthesized *N*-tosylindole, a molecule with sufficient larvicidal potency to be directed to pharmacotechnical development studies. To carry out the studies that are being proposed, this project initially aims to carry out the synthesis on a larger scale of the compound in question, followed by the development of a formulation for its use, analyzes of its cytotoxic and genotoxic potential, as well as its residual effect. Cellular and genetic toxicity analyzes will be carried out in HepG2/C3A human hepatoma cells, with extension to analyzes of effects on the cell cycle, apoptosis and expression of genes involved in these metabolic pathways. Nanotechnology will be used to obtain a formulation, aiming to increase the effectiveness of vector control and enable the use of a molecule with low water solubility, *N*-tosylindole, making this product viable for use in water. A suitable formulation must release the larvicide continuously in order to maintain the concentration of the larvicide at a high enough level to maintain its effect for a long time. The residual effect will be obtained in laboratory aiming to determine the

number of days its active ingredient stays in the environment in which it was placed. This same study can be increased to a semi-field scale, evaluating the residual effect in conditions more similar to reality in semi-field evaluation using containers in the environment. Then the formulation will be evaluated for impacts on non-target plant species *via* evaluation of *N*-tosylindole effects on germination and plant growth. At the end of the project, it is expected that the data collected will allow the use of the molecule in question as a larvicide and serve as another tool in the control of the *A. aegypti* mosquito and in the fight against the diseases vectored by it.

Start date: 12-01-2022

End date: 12-31-2024

Last modified: 04-07-2022

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Desenvolvimento e análise de toxicidade de derivado do indol com atividade larvicida frente ao *Aedes aegypti* Linn: controle da dengue, chikungunya e Zika.

Data will be obtained from three experiments listed below:

1. Formulations containing *N*-tosylindole characterized by polarized light microscopy, small angle x ray scattering, rheological analysis and Fourier-transformed infrared spectroscopy;
 2. Germination and growth of seeds exposed to different concentrations of the title compound. Number of germinated seeds, size and weight of shoots;
 3. Residual effect in laboratory and field controlled situations. Length in days the test compound produces larvicidal effect in a container with water. Number of dead larvae with time.
4. Toxicity data will be obtained from the cultured lymphocytes and HepG2/C3A human cells treated with different concentrations of *N*-tosylindol. The data will be shown the effects of these compounds in the context of cytotoxicity, genotoxicity, (with active liver metabolizing enzymes) and human leukocytes, and the effects of these compounds on the progression of the cell cycle, induction of apoptosis, and gene expression in HepG2/C3A cells (human hepatoma).

All data collected will be in tables and laboratory chains.

Formulation data will be collected using equipment mentioned before, seed germination and growth data will be collected by germinating seeds in petri dishes in controlled environment, residual effect data will be collected using beakers (lab setting) or containers (semi-field setting) containing water, formulation, and frequently added *Ae. aegypti* larvae. The data about toxicity will be collected from cultured human cells (lymphocytes and HepG2/C3A) exposed to *N*-tosylindol.

Graphics, FIDs, spectra, figures, and tables.

All procedures involving toxicity analysis will be approved by the Human Ethics Committee of the Faculty of Philosophy and Sciences, UNESP, Marília town.

Insect rearing and larvae production procedures were approved by the Ethics Committee of Animal of Federal University of Sergipe (CEPA-UFS) application # 4386260321.

As a result of this project, articles will be published. Copyright will be determined jointly with the members of our research group.

Data will be backed up with copies in hard drives in laboratory computers, as well as the university offers google Drive, which assists in data storage.

All researchers involved in the project will have access to the data, but only the researcher responsible and coordinator will edit and update the backup.

The data will be shared with the scientific community through publications. In addition, they will serve to originate future projects.

We store these data in drives of all laboratories involved in this project, and laboratory chains.

The data will be used for participation in a scientific congress. And, after a great understanding of the results, the data will be published in the form of an article or patents.

Before intellectual protection the data is not available. After intellectual protection the data cannot be used for commercial purposes without consent from the holder. Toxicity data will be published for the entire community, after which it can be shared.

The data acquired during the project will be managed by the responsible researcher in each laboratory and the project coordinator.

The project will be necessary for collaboration with other researchers to collect and analyze the data obtained from the mentioned experiments.
