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Challenges in the Use of Secondary Metabolites of Endophytic Fungi for the Control of Aedes Aegypti (Linnaeus, 1762)

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Editorial

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Editorial

The *Aedes aegypti* mosquito, whose name means "the odious one of Egypt," originated in Africa. Described in 1762 by Linnaeus, it has become the most widely and globally distributed mosquito species. It is a vector of the viruses that cause dengue fever, urban yellow fever, Zika, and chikungunya. In Brazil, *A. aegypti* was probably introduced in the 16th century as maritime trade routes expanded, together with the slave trade. Since the 1930s and the 1940s, eradicating the vector in the Americas has been pursued intensively, supported mainly by the Rockefeller Foundation [1]. However, eradication is practically impossible because of the biology and genetic plasticity of the mosquito combined with new artificial breeding sites and synanthropy of this species.

Dichlorodiphenyltrichloroethane (DDT) is one of the first chemical compounds with a prolonged effect on the control of mosquitoes, the use of which began in the 1940s and 1950s. Its use in eradication campaigns financed by the Pan American Health Organization was considered successful in controlling *A. aegypti,* and the species was considered eradicated in Brazil by 1958 [1]. However, in the ensuing decades, new outbreaks appeared. This has prompted efforts by government agencies and public/private research institutions to find definitive and sustainable controls.

These efforts have included the use of synthetic insecticides based on organophosphate compounds, carbamates, and pyrethroids. However, the use of these compounds is associated with many adverse and toxic environmental effects, human health risks from residual compounds, and high rates of resistance development in insects [2,3]. In Brazil, a commonly used adulticide comprises a mixture of pyrethroid and neonicotinoid. Larvicides, growth regulators, and spinosad are also used of these agents, *Bacillus thuringiensis israelensis* is most selective, with no evident adverse effects to fauna and humans.

The preceding issues emphasize the need for new strategies to combat *A. aegypti* in immature or adult forms using compounds that are less polluting, less toxic, and less harmful to human health. Several studies involving bioactive natural products have indicated the potential of endophytic fungi [4]. Studies have successfully evaluated the larvicidal activity of secondary metabolites of endophytic fungi against *A. aegypti*. One of the first of these studies was conducted in the early 1990s. Since then, many endophytic fungi have been tested, including fungi from the genera *Penicillium, Aspergillus, Fusarium, Hyalodendriella, Cochliobolus, Phomopsis, Berkleasmium, Pezicula,* and *Pestalotiopsis.*

The fermentation process for fungi is short, simple, and economically viable. Recent and dynamic progress in fermentation, extraction, purification, and characterization techniques facilitate rapid characterization of new natural products and efficient access to endophytic resources. However, there are several challenges in conducting secondary metabolite bioassays against *A. aegypti.* Improvement of

microorganism strains through genetic engineering to obtain a greater volume of active and selective secondary metabolites for the target species is one challenge. The suitability of the microorganisms for industrial applications is another challenge. It is also necessary to understand the biosynthetic pathway of microorganisms to identify how bioactive compounds are produced, thereby facilitating reproduction by conventional production systems and production of target compounds with ease.

Laboratory mosquito tests with both the *A. aegypti* Rockefeller strain and the laboratory samples obtained in the field are necessary to validate the lethal concentrations of fungal metabolites on the mosquito. Furthermore, for subsequent application under simulated field conditions, mortality of the associated fauna must be verified to validate the metabolites and comply with regulatory requirements for field applications.

The discovery of new secondary metabolites, bioassay performance, and future tests in natural environments are necessary. In addition, collaborations between microbiologists, entomologists, and biotechnologists are essential to produce effective formulations at an industrial scale. The search for sustainable alternatives for the control of *A. aegypti* is ongoing since currently few molecules are available.

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