Alteration of the mitochondrial respiratory chain and induction of oxidative stress on larvae of *Aedes aegypti* by Girgensohnine analogs

Borrero, M.[1, 3], Méndez, S.[1], Carreño, A. [2,3], Kouznetsov, V.[2] Duque, J.[3]

[1] Grupo de Investigación en Bioquímica y Microbiología (GIBIM) Escuela de Química. Universidad Industrial de Santander, Colombia. [2] Laboratorio de Química Orgánica y Biomolecular (LQOBio) Escuela de Química. Universidad Industrial de Santander, Colombia. [3] Centro de Investigación en Enfermedades Tropicales (CINTROP) Escuela de Medicina, Departamento de Ciencias Básicas, Universidad Industrial de Santander, Colombia.

Introduction: Dengue, Chikungunya and Zika are diseases transmitted by the *Aedes aegypti*, which are widely distributed in tropical and subtropical areas worldwide. Since there is no vaccine, disease control is limited to the vector control. Therefore, currently novel compounds that can act as insecticides and which in turn are friendly to the environment are studied. **Objectives:** The objective of this work was to evaluate the insecticidal activity of a series of analogs (α-aminonitriles of girgensohnine alkaloid) through it inhibitory activity over enzyme complexes in the mitochondrial respiratory chain (MRC) and the antioxidant enzymes catalase and superoxide dismutase (SOD) from Aedes aegypti larvae. **Material and methods:** Mitochondria were isolated from larvae between third and fourth instars, using a Van Potter homogenizer to disintegrate the biological material. The suspension was subjected to differential centrifugations, and the mitochondria obtained were fragmented by ultrasound. The enzyme activities of mitochondrial electron transport chain were assessed by spectrophotometric and polarographic methods. For measurement of the antioxidant enzyme activity, the whole protein fraction obtained in the first centrifugation step was used. All inhibition assays were done using 8nM, 2 µM, 8 µM and 40 µM of each analog. **Results and discussion:** The results indicate that the analogs cause significant inhibition of enzyme activity of the NADH dehydrogenase (44% with 40µM). The succinate dehydrogenase and cytochrome c oxidase activities were increased (162% and 106% with 40µM, respectively). It was found that the compounds in the highest concentration cause inhibition of the catalase (95%), inhibition of SOD (50%) and an increment in the production of superoxide radical in a protein-free system. **Conclusion**: The compounds tested showed inhibition on mitochondrial respiratory chain complex I, promoting the release of electrons and the formation of reactive oxygen species. This was checked by the inhibition of catalase, SOD and the increment of superoxide radical.

Keywords: *Aedes aegypti*, mitochondrial bioenergetics, girgensohnina, oxidative stress.