Antihyperglycemic Activity of the Leaves from *Annona diversifolia* Safford and Farnesol on Alloxan-Induced Type 2 Diabetic Mice

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Background: Several species of the Annonaceae family are used in Mexico as a treatment for the diabetes mellitus, some species like *Annona cherimola*, *Annona reticulata*, *Annona squamosa* and others have phytochemical studies that demonstrate the antidiabetic activity but theres no studies on *Annona diversifolia*, in this sense, the aim of this study was to investigate the antihyperglycemic effects of a Mexican traditional plant, *Annona diversifolia*, on alloxan-induced type 2 diabetes mellitus (AITD) and normoglycemic mice and to explore its potential as an alpha-glucosidase inhibitor.

Methods: For the development of DM, a single dose IP of alloxan (150 mg/kg) was used. In the acute test, oral glucose tolerance assay (OGTA) and oral sucrose tolerance assay (OSTA) the products were administered intragastrically and the glycemia values were measured at 2 and 4 hours, for the subchronic test the products were administered daily and the glycemia values were measured once a week during 28 days. The administration of the ethanol extract of the leaves from *Annona diversifolia* (EELAd, 200 mg/kg, 300 mg/kg, and 600 mg/kg), subsequent fractions (200 mg/kg), and farnesol (50 mg/kg) were given to AITD and normoglycemic mice. Also, OGTA and OSTA were performed in normoglycemic mice.

Results showed that the EELAd, (200 mg/kg), CHCl₃ fraction (CF), and farnesol induced a significant decrease of postprandial hyperglycemia in acute tests using AITD mice, with maximum effect at 4 h. The antihyperglycemic properties of EELAd, CF, and farnesol were like with acarbose an alpha-glucosidase inhibitor. In the subchronic assay on AITD mice, of the EELAd, CF, and farnesol showed a reduction of the glycemia levels since the first week of treatment reaching levels similar to normoglycemic state that stayed constant for the rest of the test. OGTA and OSTA showed that the EELAd, CF, and farnesol significantly lowered glycemia levels in normoglycemic mice at 2 h after a glucose or sucrose load like to acarbose.

Conclusions: Our work showed that the EELAd, CF, and farnesol could alleviate the type 2 diabetes mellitus and maintain the glucose homeostasis in AITD mice like to alpha-glucosidase inhibitor and would be one of its possible underlying mechanism.