HEPATOPROTECTIVE EFFECT OF HYDROALCOHOLIC EXTRACT FROM EDIBLE ROOT OF *Sechium edule* (Jacq.) Sw. INDUCED BY CHRONIC APPLICATION OF AGII IN MICE.

Gabriela Rosas Salgado[1*]; Zimri Aziel Alvarado-Ojeda[1]; Alejandro Costet Mejía[1]; Gerardo Arrellín Rosas[1,2]; Jesús Enrique Jiménez-Ferrer[3]; Alejandro Zamilpa[3]; Celeste Trejo-Moreno[4]; Gabriela Castro-Martinez[1]; Jacquelynne Cervantes Torres[5]; Juan Carlos Báez Reyes[6]; Gladis Fragoso[5].

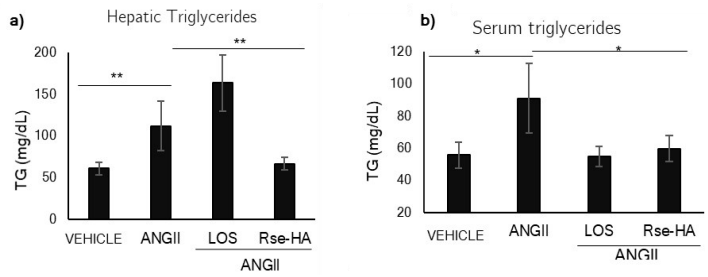
[1] Facultad de Medicina, Universidad Autónoma del Estado de Morelos, Leñeros S/N, Cuernavaca, Morelos; México; 62350, zimrihazi@gmail.com; alejandro.costet@gmail.com; gabriela.rosas@uaem.mx.
[2] Facultad de Ciencias de la Salud, Universidad Panamericana, Ciudad de México, México, 03920, garrellin@up.edu.mx
[3] Laboratorio de Farmacología, Centro de Investigaciones Biomédicas del Sur, Instituto Mexicano del Seguro Social, Xochitepec, Morelos 62790, México; azamilpa_2000@yahoo.com.mx; enriqueferrer_mx@yahoo.com; gcm_19@hotmail.com
[4] Estancia Posdoctoral en el Posgrado en Biología Experimental, Universidad Autónoma Metropolitana-Iztapalapa, Ciudad de México, México, 09340, trejomc@hotmail.com
[5] Departamento de Inmunología, Instituto de Investigaciones Biomédicas, Universidad Nacional Autónoma de México, Coyoacán, Mexico City, México, 04510; jcervantes@iibiomedicas.unam.mx; gladis@unam.mx
6 Escuela Nacional Preparatoria No.1 UNAM Av. De la Noria y Calle Prolongación de Aldama s/n Tepepan Xochimilco. 16020, Ciudad de México;

INTRODUCTION: Non-alcoholic steatohepatitis (NASH) is characterized by lipid accumulation, a pro-oxidant and proinflammatory status, necrosis and fibrosis which conduce to hepatic carcinoma and cirrhosis[1,2]. In 2018, we assessed the activity of *S. edule* extracts in a mouse model of ED induced by a chronic administration of ANGII[3] and observed that the acetonic fraction of an S. edule extract not only controlled ED and hypertension, but it also prevented hepatic fibrosis and steatosis[3]. The Hydroalcoholic extract from Sechium edule root (HArSe) standardized in cinnamic acid, was used to control the establishment of NASH in mice .

OBJECTIVE : This work is aimed to demonstrate the hepatoprotective capacity of hydroalcoholic extract of roots of S. edule, standardized in cinnamic acid in a murine model of NASH, induced by a chronic administration of ANGII.

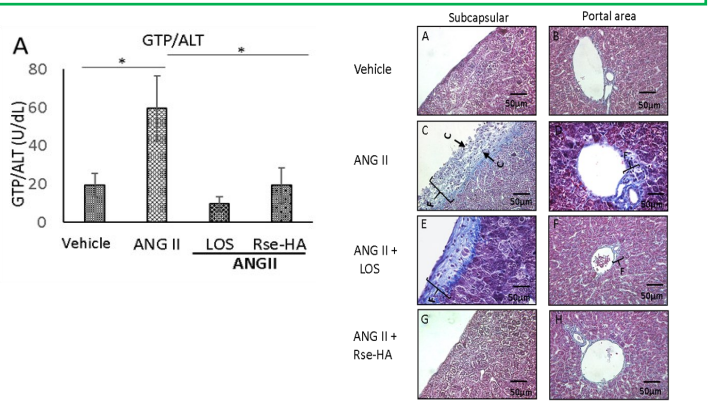
MATERIAL AND METHODS: C57/BL6 male mice were treated daily with AGII (0.01 µg/Kg/day I.P) AND WITH 11 mg/Kg/day of HArSe, orally administered. After 11 weeks the mice were sacrificed and serum and liver and were obtained. Histopathological studies were performed in the liver, and concentration of cytokines and triglycerides (TGs) were measured also in liver. Concentration of alanine aminotransaminase (GPT/ALT). was measured in sera.

RESULTS:
ANTI-STEATOSIS AND ANTI-HIPERTRIGLICERIDEMIC EFFECT OF RSE-HA.



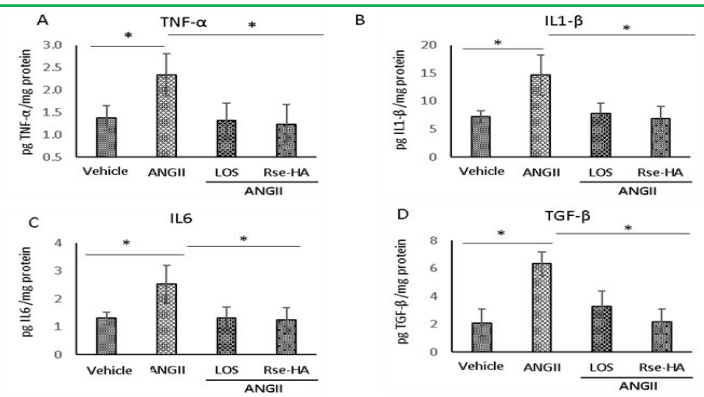
ANTI-STEATOSIS AND ANTI-HYPERTRIGLYCERIDEMIC EFFECT OF RSE-HA: Hepatic an Serum TG levels in mice that received different treatments for 11 weeks. Vehicle-administered group (Vehicle); group administered with ANGII (i.p., 0.01 µg/kg/day) (ANGII); group treated with ANGII + LOS (10 mg/kg/day) (LOS); group treated with ANGII + Rse-HA (11 mg/kg/day) (Rse-HA). Results are expressed as the mean ± SD and were analyzed by one-way ANOVA and a post-hoc Tukey test. $*P < 0.05$; $**P < 0.01$;with respect to the ANGII group.

RSE-HA PREVENTS HEPATIC FIBROSIS AND NECROSIS.



ANTI-FIBROTIC AND ANTI-NECROTIC EFFECT OF RSE-HA: Bar chart A) shows GPT/ALT levels in serum samples from mice that received different treatments for 11 weeks. Histopathological analysis showing A, B) Vehicle-treated mice; C, D) Mice treated with ANGII alone (0.01 µg/kg/day); E, F) Mice treated with ANGII + losartan (10 mg /kg/day); G, H) Mice treated with ANGII + Rse-HA (11 mg/kg/day). Results are expressed as the mean ± SD and were analyzed by one-way ANOVA and a post-hoc Tukey test. *P < 0.05; **P < 0.01; with respect to the ANGII group. Microphotographs were taken at 10 and 40X. F = collagen fibers in subcapsular and portal areas. Arrows (C) indicate inflammatory cells in the subcapsular area.

ANTI-INFLAMMATORY EFFECT OF RSE-HA



ANTI-INFLAMMATORY EFFECT OF RSE-HA : A-D shown the concentrations of cytokines TNFα, IL1β, IL6, and TGFβ in liver samples from mice that received different treatments (vehicle, ANGII, ANGII+Losartan, or ANGII+Rse-HA) for 11 weeks measured by ELISA. P< 0.05

CONCLUSION.

The standardized extract from the roots of *Sechium edule* prevented hypertriglyceridemia, increase of adipose tissue and hepatic alterations as steatosis, hepatomegaly, necrosis, inflammation, and fibrosis induced by chronic application of AGII.

REFERENCES

1- Rolo A.P., Teodoro J.S., Palmeira C.M. Role of oxidative stress in the pathogenesis of nonalcoholic steatohepatitis. Free Radic Biol Med, 2012, 52(1), 59-69. doi:10.1016/j.freeradbiomed.2011.10.003
2.-Karlas T., Wiegand J., Berg T. Gastrointestinal complications of obesity: non-alcoholic fatty liver disease (NAFLD) and its sequelae. Best Pract Res Clin Endocrinol Metab. 2013, 27(2), 195-208. doi:10.1016/j.beem.2013.02.002
3.-Trejo-Moreno C.., Castro-Martínez G., Méndez-Martínez M., et al. Acetone fraction from Sechium edule (Jacq.) S.w. edible roots exhibits anti-endothelial dysfunction activity. J Ethnopharmacol. 2018, 220, 75-86. doi:10.1016/j.jep.2018.02.036