glycolytic pathway and the traditional Warburg effect. Then we evaluated if the Huh-7 under a Fru treatment was more dependent on mitochondria or glycolysis ATP generation. We observed a reduction in proliferation under oligomycin treatment *vs*. 2-DG treatment. At least, we evaluated the pentose phosphate pathway (PPP) under a Fru treatment and obtained a higher glucose-6-phosphate dehydrogenase (G-6-P DH) activity with Fru *vs*. only glucose (Glc). Also, G-6-P DH had a more efficient activity in the presence of Fru because the time to reach the Vmax is lower *vs*. Glc.

Conclusion: Fructose induces a metabolic rewiring in cancer cells to enhance ATP production, NADPH, and nucleotides to sustain the active lipid synthesis and proliferation. The fructose-enriched diets promote an aberrant lipogenic phenotype enhancing tumor aggressiveness. Conacyt, Froteras de la Ciencia 1320.

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ANTIOXIDANT EFFECT OF SPINACH EXTRACT IN LIVER FIBROGENESIS ASSOCIATED TO ACTIVATION OF NRF2/HO-1 IN HYPERGLYCEMIC RATS

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Introduction and Objectives: In chronic hyperglycemia, increased oxidative stress plays an essential role in liver fibrogenesis. The spinach phytochemicals are shown to possess chemopreventive properties in this condition. Erythroid nuclear transcription factor 2 (Nrf2) is a transcriptional regulator expressing cytoprotective genes such as heme oxygenase-1 (ho-1). HO-1 is an enzyme present in the liver with antioxidant, anti-inflammatory, and anti-apoptotic capacities. However, the beneficial effect of spinach associated with endogenous activation of the Nrf2/HO-1 pathway is unknown. Objective: To evaluate the antioxidant effect of the spinach extract on injury hepatic associated with the Nrf2/HO-1 pathway in hyperglycemic rats.

Materials and methods: The study was approved by the ethics committee from the ENCB-IPN (CONBIOETICA/09/CEI/002/20190327). We used hyperglycemic Wistar rats induced with 60 mg / kg of streptozotocin (HG; n = 7); intragastrical-treated HG with 400mg / kg of spinach methanolic extract (HG-EME; n = 7) and normoglycemic rats (NG; n = 7). Histological sections were obtained at 12 weeks and evaluated by Sirius red staining and immunohistochemistry (Nrf2, HO-1). The oxidative damage by lipid peroxidation was determined by the tissues' malonaldehyde formation (MDA) levels. The H-score system quantified the percentage of nuclear staining of Nrf2 and the intensities of Sirius red and HO-1. Statistical analysis: The data were analyzed by one-way ANOVA with the Tukey test using the GraphPad Prism program (Version 5.0). Kruskal-Wallis and Dunn's test established the MDA training levels. Statistical significance was considered with $p < 0.05$.

Results: Collagen fibers were formed mainly in the centrilobular zone. The percentage of collagen fibers staining in the HG group was 50 ± 10, compared to HG-EME (30 ± 10 $p < 0.05$). In NG, the percentage of fibers was 20 ± 10. The nuclear Nrf2 (nNrf2) and cytoplasmic HO-1 staining were localized in the hepatocytes of region 3 Rappaport. The percentage of nNrf2 in HG was 30 ± 10, compared to HG-EME (70 ± 10 $p < 0.01$). In NG, the staining percentage for nNrf2 was 15 ± 5. For HO-1 staining, the values in the HG-EME group were higher than in the HG group ($p < 0.01$). Contrary, MDA levels in HG-EME decreased significantly compared to HG ($p < 0.05$).

Conclusions: Treatment with EME in hyperglycemic rats showed decreased liver damage generated by oxidative stress, associated with endogenous activation of the Nrf2/HO-1 pathway. The evaluation of liver biochemical tests can demonstrate a beneficial effect of EME. This work was supported by federal resources (HJM0713/19-I) and partially by INCICH.

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NAMPT INHIBITION AND INCREASED NAD-BIOAVAILABILITY ATENUATE LIVER DAMAGE IN CCl_4-INDUCED MICE CHRONIC LIVER DISEASE

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Introduction and Objectives: Nicotinamide phosphoribosyltransferase (NAMPT) is the rate-limiting enzyme on the NAD^+ salvage biosynthetic pathway and a cytokine regulator with an important role in inflammation and fibrogenesis modulation. Use of FK866 (NAMPT inhibitor) has been proposed as a treatment on inflammatory diseases and cancer. However, FK866-induced depletion of NAD may also cause major impairment of the redox and bioenergetics homeostasis of the cell within the liver, thus limiting a favorable outcome for Chronic Liver Disease (CLD), as low NAD levels have been associated with higher Oxidative Stress and increased metabolic risk. The aim of this study was to evaluate the effects of NAMPT inhibition and concomitant NAD restoration on experimental CLD in vivo.

Methods and Results: NAMPT inhibition was evaluated within a CCl_4-induced CLD model on male BALB/c mice and a mild improved outcome was observed on the histological and biochemical features. NAD restoration strategy was accomplished by the concomitant administration of its precursor, NMN, resulting in significant improve on the histological analysis; lower inflammatory infiltrate and fibrosis were measured by image analysis on digitalized micrographies. Lower levels of Direct Bilirubin were also observed. NAMPT inhibition and adequate NAD restoration were confirmed by a colorimetric assay of NADH and NAD^+ and biochemical features were measured by routinary Liver Function Tests. Silymarin was used as a hepatoprotective control.

Conclusion: This study shows that NAMPT inhibition concomitant to NAD restoration significantly attenuate experimental liver damage.

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