cognitive parameters, obtaining higher Discrimination Index than the ND group in test novel object recognition (NOR).

Discussion: Supplementation with nopal or cocoa has been shown to reduce alterations caused by a diet high in fat and sugar; however, the simultaneous supplementation proposed in this project induced more noticeable benefits, being similar to those achieved with a switch from HF diet to ND diet.

Conclusions: MexTHER supplementation is a potential strategy for the treatment of diseases associated with excessive consumption of fat and sugars, such as MAFLD.

The authors declare that there is no conflict of interest.

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EVALUATION OF THE HEPATOPROTECTOR EFFECT OF A SUPPLEMENT WITH CURCUMA LONGA AGAINST REPERFUSION ISCHEMIA DAMAGE IN AN EXPERIMENTAL MODEL IN WISTAR RATS

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Introduction and Objectives: Liver transplantation (LT) is the treatment for end-stage liver disease that may present graft rejection. Conditioning with natural products has shown great therapeutic utility, specifically against ischemia-reperfusion (IR). Curcumin has shown protective activity, which is why it is proposed to evaluate whether curcumin (AGROVITAE-UANL) reduces IR liver damage.

Material and methods: For thin layer chromatography, curcumin was started in 0.1% methanol using Si-60GF254 silica gel and chloroform: methanol (95: 5). To verify the presence of 3 curcuminoids, delay factors (Rf) equal to the curcumin standard (Sigma-Aldrich) were detected. For the 70% partial IR liver damage model, a midline laparotomy (L) was performed, the liver was dissected, the hepatic hilum clamped for 1 hour of IR and subsequent sacrificed by exsanguination. 4 groups were established: Sham (3% Tween 20; 500 μL x 3 days; L); IR (3% Tween 20; 500 μL x 3 days; L + IR); SIGMA + IR (3% Tween 20; curcumin 200 mg / kg x 3 days; L + IR); AGROVITAE+IR (3% Tween 20; curcumin 200 mg / kg x 3 days; L+IR). ALT, AST, LDH, FA, BIL, PT, ALB, MDA and Total Antioxidants (AOT) were quantified by UV-Vis. NF-kβ and MPO were evaluated by RT-qPCR. The protocol approved by the ethics committee with registration PI20-00002.

Results: The Rf of 3 curcuminoids was calculated: Curcumin (0.80), Demethoxycurcumin (0.69) and Bisdemethoxycurcumin (0.62). In the damage model, a significant increase in ALT, AST and LDH was achieved and a hepatoprotective effect against IR damage due to decreases in liver enzymes (Figure), there was no change in the rest of the markers.

No significant difference was found in the oxidative stress markers MDA and AOT and in the gene expression of NF-kβ and MPO associated with IR.

Discussion: Reyes et. al (2014) reported the presence of the 3 curcuminoids and their Rf, which agrees with our results. Wang et al. (2017) reported a decrease in ALT and AST values in the groups treated with curcumin in a partial IR model, which is consistent with this study. Lintz et al. (2017) reported in a partial IR model that LDH may not be affected, this contrasts with our results; however, in the curcumin groups, no significant difference was observed against IR. Zabala et al. (2019) reported elevation of ALT and AST that agrees with what was obtained in this study. Tinsay et al. (2014) reported that in IR, there was no effect on synthesis and cholestasis markers, as in this study, this can be explained because the damage produced is cell lysis. Regarding the non-difference in the gene expression of NF-kβ and MPO, other authors reported that the regulation of inflammatory response genes would have an effect at longer reperfusion times (3, 6, 12 and 24h), in hepatic partial IR models.

Conclusions: The presence of the 3 curcuminoids was confirmed in AGROVITAE-UANL. The IR damage model was effective in increasing ALT, AST, and LDH. A hepatoprotective effect of AGROVITAE-UANL, against IR by decreasing ALT and AST. No effect was observed on liver synthesis markers or cholestasis, so the damage was only associated with cell lysis. There was also no effect on MDA, AOT markers and inflammatory response genes at the established IR times, ruling out these pathways as possible mechanisms of action.

The authors declare that there is no conflict of interest.

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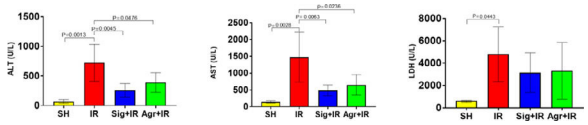

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CHEMOSENSITIZING EFFECTS OF GDF11 IN HUMAN HEPATOCELLULAR CARCINOMA CELLS

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Introduction and Objectives: Hepatocellular carcinoma (HCC) ranks as the second leading cause of cancer death globally; this neoplasm accounts for approximately 90% of liver cancers, and about 850,000 new cases are reported annually. Several factors increase the likelihood of developing HCC, such as excessive alcohol consumption, hepatitis B and C virus infection, metabolic syndrome, and a diet high in lipids and cholesterol. The chronic lesions that the liver can suffer due to the aggression of these factors usually generate lower grade pathologies such as fatty liver, hepatitis, and cirrhosis, which can evolve into HCC. In 2019 Gerardo-Ramirez and collaborators from our group reported the ability of GDF11 to subtract aggressiveness to several HCC-derived cell lines HCC (Huh7, Hep3B, SNU-182, Hepa 1-6 and HepG2); they found that GDF11 reduced proliferation, metastatic capacity, colony, and spheroid formation and invasiveness in those cell lines. Findings by Gerardo-Ramirez *et al.* (2019) identified transcriptional repression of cyclins D1 and A and overexpression of p27. Additionally, an increase in the expression of epithelial markers E-

cadherin and Occludin was observed; conversely, mesenchymal-type features such as N-cadherin and Snail decreased with GDF11 treatment, confirming that this growth factor-induced a mesenchymal to epithelial transition. Furthermore, our group reported the effect of GDF11 in reducing lipid content, especially cholesterol and triglycerides. It was also confirmed that GDF11 reduced mevalonate pathway proteins in Huh7 and Hep3B liver cancer cell lines. Additionally, they reported that GDF11 was able to impair mitochondrial functionality and its structure. Moreover, GDF11 treatment induced an alteration of glycolytic capacity and oxygen consumption rate in these models.

Objectives General: To determine the sensitizing effect of GDF11 in the Hep3B cell line. Specific: To determine the capacity of GDF11 in the reduction of the EC50 of cisplatin.

Methods: We used the HCC cell line Hep3B (ATCC). A 72-h pretreatment with GDF11 or without was performed; then we treated the cells with cisplatin at various concentrations (0, 2.5, 5, 10, 15, 15, 25, 50, and 100 μM), incubated for 48 h, and cell viability assay was performed by crystal violet.

Results: In our experiments, GDF11 has shown an increased sensitivity of Hep3B cells to cisplatin treatment by significantly reducing the mean effective dose (EC50) from 22.26 μM to 8.11 μM this result was observed by crystal violet assay and by light microscopy.

Discussion: Results demonstrate that GDF11 has sensitizing effects against cisplatin treatment on the liver tumor cell line Hep3B. This agrees with previous results of our group where a detrimental impact in liver tumor cells is observed by the GDF11 treatment and contrast with other works where TGF-β family members have chemoresistance effects.

Conclusions: GDF11 pretreatment sensitizes the HCC cell line Hep3B by reducing the cisplatin EC50.

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HGF AND PROTECTIVE ROLL IN THE INTESTINAL COLLATERAL DAMAGE BY A-NAFTILISOTIOCIANATO- INDUCE CHOLESTASIS.

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Introduction and Objectives: he prevalence of cholestasis has been increasing in recent years; The excretion of bile acids via basolateral has been demonstrated to prevent the excessive accumulation in the hepatocyte, and the liver-intestine axis has been seen affected by enterohepatic circulation deregulation. The epithelial permeability loss caused by the tight junction ruptures leads to inflammation and reactive oxygen species (ROS) production. The hepatocyte growth factor is an essential cellular redox regulator and repair growth factor; it has been reported in its relevance in the intestinal mucosa regeneration and proliferative proprieties. This study aims to evaluate the protective effect of HGF in the intestine of animals subjected to cholestatic damage induced by ANIT. Material and methods: Twenty 10-12 weeks-old male CD-1 mice were used. ANIT (60mg/kg) was administrated at the beginning, 24 h later HGF (10 μg/kg) was injected, and 48 h later, the animals were subjected to euthanasia under anesthesia, and serum and intestines were collected. According to the National Institutes of Health of United Stated (NIH) guide, All mice have been cared for and the Norma Oficial Mexicana (NOM), NOM-062-ZOO-1999. The intestinal tissue was fixed and embedded in paraffin for the histological assessment, followed by routine H&E staining. The expression analysis of TNF- alpha, IL-1b and IL.6 were performed by RT-qPCR using a CFX96 Touch thermocycler with 5μg 2x SYBER Green, which included 1000ng of cDNA and 2μl of forward and reverse primers. The protein quantification was evaluated by Western Blot analysis; using 12% polyacrylamide gels, and the primary antibodies for anti-SOD-1, anti-GPx4, anti-Catalase were incubated. Data are presented as the average $\pm$ standard error media (SEM) using GrandPad (Prism 8) software. Variance analysis (ANOVA) was used for the statistical analysis and was considered $p<0.005$ to indicate a statistical significance.

Results and Discussion: Macroscopic changes reveal no apparent effect. Microscopic studies carried out by H&E staining showed a reduction of the intestinal lumen diameter in mice under ANIT treatment compared with Not treated control (NT). Interestingly, ANIT + HGF-treated group showed protective effects preserving lumen and tissue architecture. To corroborate the potential repair effect of HGF treatment to maintain the tissue and thus digestive process, the excreted stool for every group was addressed. The stools excretion level of ANIT- treated mice was significantly reduced compared with the control and co-treated mice. These results indicate that ANIT-cholestasis induce damage in the small intestine. However, results also found a vulnerability in the colon and ileum to cholestasis damage. To determine whether these sections received damage in ANIT- acute cholestasis model, by RT q-PCR, we examined the mRNA expression of inflammatory cytokines, which were increased in ANIT- treatment. By comparison, HGF co-treatment decreases inflammation like the control group. To check if this regulation of inflammation was for the HGF-induced redox regulation we evaluated, the protein expression of SOD-1, GPx4, and catalase. The treatment with HGF increased the expression of antioxidant enzymes of the intestine tissue. These results suggest that the damage in the intestine is supported by the regulation of ROS induced by cholestasis disease.

Conclusion: The current study demonstrated how HGF exerts a protective effect in the intestine triggered by ANIT. This effect seems to be the cellular redox regulation seen in the liver and renal tissue.

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IGFBP-1 TO 7 AS BIOMARKERS IN STAGES OF LIVER FIBROSIS DURING VIRAL HEPATITIS C

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