Materials and Methodology: Huh 7 cells were transfected with an empty vector, and 0.5 - 1.0μg of pNluc-NS5A-HCV or pCore-HCV plasmids for 24 - 48h and then proteins and RNA were extracted. NS5A protein expression was measured by NanoLuc activity. Core, Snail, TGFβ1 and E-cadherin protein levels were evaluated by Western Blot. NS5A and Core transcripts were quantified by RT-qPCR. Relative expression of SNAI, TGFβ1 and CDH1 was calculated in relation to ACTB and GAPDH endogenous expression.

Results: Viral NS5A and Core proteins were expressed in transfected Huh 7 cells. Transient transfection with pNluc-NS5A-HCV upregulated snail expression (4-fold) but downregulated E-cadherin expression (0.6-fold) at 24h. In addition, upregulated TGFβ1 expression (4-fold) and downregulates E-cadherin expression (0.7-fold) at 48h compared to the control. Meanwhile, transfection of pCore-HCV for 24h upregulated snail expression (2-fold); in contrast, it downregulated E-cadherin expression (0.3-fold) compared to control at 48h.

Discussion: Snail and TGFβ1 upregulation and E-cadherin downregulation had been associated with HCV infection in other studies. Our results suggest that HCV NS5A and Core have a direct role in EMT.

Conclusion: Hepatitis C virus regulates epithelial-mesenchymal transition biomarkers by NS5A and Core proteins expression in hepatoma cells.

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Diethylnitrosamine and 2-acetylaminofluorene chronic administration leads to biochemical and histologic changes related to hepatocellular carcinoma in Wistar rats

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Introduction and Objectives: This study aimed to analyze the biochemical and histological alterations produced in a model of chemical hepatocarcinogenesis by the chronic administration of diethylnitrosamine (DEN) and 2-acetylaminofluorene (2-AAF) in Wistar rats.

Materials and methods: Twelve Wistar rats weighing 180 to 200 g were divided into control and damage groups: rats were treated with DEN (50 mg/kg/wk) i.p and an intragastric dose of 2-AAF (25 mg/kg/wk) for 18 weeks. Serum clinical biochemistry was performed on VITROS Chemistry System 350® equipment. Masson's trichrome and Hematoxylin-Eosin stains were performed on the liver tissue. The trial was approved by the research ethics committee.

Results: The damage group had significant increases in total cholesterol, HDL-C, AST, ALT, ALKP, and GGT. Furthermore, histological analysis showed the loss of normal liver architecture with nuclear pleomorphism in the hepatocytes, atypical mitosis, and fibrous septa distributed between portal triads and collagen fibers through the hepatic sinusoids.

Discussion: Hepatocellular carcinoma models are a valuable tool to identify alterations during the progression of the disease. The Fischer-344 strain is frequently used in chemical hepatocarcinogenesis models since this strain shows greater susceptibility to the development of liver tumors. The damage induction model used in this work causes advanced hepatocellular carcinoma in Wistar rats, in spite of being a strain with intermediate susceptibility to hepatocarcinogenesis. The damage was evidenced by the presence of hepatomegaly, fibrosis, abundant nodules, histological changes, and biochemical alterations.

Conclusion: Chronic administration of DEN and 2-AAF induces characteristic alterations of hepatocellular carcinoma in Wistar rats.

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In vitro evaluation of the antifibrogenic effect of tamsulosin during its interaction with activated stellate cells

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Introduction and Objective: Liver cirrhosis is a chronic disease that affects one-fifth of the world; in Mexico, it is the third cause of mortality. It is caused by the uncontrolled production of the extracellular matrix. Attempts have been made to develop treatments that can reverse this disease, attention has been paid to the stimuli responsible for the activation of hepatic stellate cells (HSC), and the presence of adrenoreceptors in these cells has also been demonstrated. This study aimed to demonstrate in the present work a possible treatment with a neuroimmune activity that decreases the fibrogenic capacity of HSC.

Material and Methods: Rat's HSC in a quiescent state and activated by primary culture were used. Cells in a quiescent state contain retinol and lose it by activation. The degree of activation was assessed by immunofluorescence for α-SMA and cytochemistry with Oil Red. Cell proliferation was assessed by the MTT reduction technique. Norepinephrine was used to activate adrenergic signaling and tamsulosin was used as an antagonist of this pathway.

Results: Initially, we standardized the primary culture of HSC, identified by the α-SMA marker at seven days of culture. Subsequently, it was demonstrated that Noradrenaline treatment activated stellate cells due to the progressive increase of α-SMA and its proliferation. Moreover, tamsulosin treatment was shown to decrease retinol loss by preventing its activation and reducing proliferation.

Conclusion: Tamsulosin has a direct effect on decreasing the activity of quiescent and activated HSCs.