Regarding SADR, there was a higher number in the GLE/PIB group (14) vs. SOF/VEL group (4) ($p<0.05$). 84% (16/18) of patients with SADR had a multi-DDI profile. 13% of total multi-DDIs patients showed SADR; GLE/PIB group showed SADR in 18% (13/71) vs 6% (3/52) in SOF/VEL group ($p<0.05$). Most SADR were reported in statin group, percentage higher in the GLE/PIB group vs. SOF/VEL group ($p<0.05$).

Both pDAAs showed a similar percentage of patients restarting a new pDAA within six months after the end of treatment (1.0% and 1.1%, respectively, p=NS).

Conclusions: In Spain, about 10% of HCV patients taking ≥ 2 comedications are at risk of multiple DDI with pDAAs. The potential risk of increased comedication as DDI outcome and the presence of suspected adverse reactions were higher in GLE/PIB in comparison with SOF/VEL.

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P- 25 ANTIOXIDANT EFFECT OF MORINGA OLEIFERA IN A MURINE MODEL OF NONALCOHOLIC STEATOHEPATITIS

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Introduction and Objectives: One of the main mechanisms in the development and progression of nonalcoholic steatohepatitis involves oxidative and endoplasmic reticulum stress. Several studies have reported therapeutic effects of Moringa oleifera leaf extracts in different animal and cellular models due to their antioxidant, anti-inflammatory and lipid-lowering effects. This study aimed to evaluate the effect of Moringa oleifera aqueous extract on biomarkers of oxidative stress in a murine model of non-alcoholic steatohepatitis.

Material and methods: Characterization of the aqueous extract was performed by DPPH and ABTS spectrophotometric assays. Male C57BL/6J mice were randomized into two groups. 1) Conventional diet (ND) (n = 5) (18% lipid) and 2) High-fat diet (HF) (n = 10) (60% lipid and 42 g/L sugar in water of use) for 16 weeks. On the ninth week, five animals in the HF group were divided into a subgroup, 3) Moringa Oleifera (HF + MO), 290 mg/kg/day p.o. for eight weeks. Malondialdehyde (MDA) levels were determined in liver homogenates and the transcriptome was measured by microarrays. miRNAs involved in liver disease were also determined. Statistical analysis was performed by differences between groups determined by ANOVA or Kruskal-Wallis test.

Results: Moringa aqueous extract showed antioxidant capacity; DPPH values were 10081.4 ± 0.3 and 22960.4 ± 0.3 for ABTS. Hepatic MDA levels increased in the HF group compared to the ND group ($p<0.05$) and decreased in the moringa-treated group ($p<0.05$). The transcriptome analysis demonstrated the downregulation of genes involved in endoplasmic reticulum stress. The miR-122-5p, miR-21a-5p, miR-34a-5p and miR-103-3p decreased in the MO-treated group.

Conclusions: Moringa oleifera treatment might be considered a therapeutic alternative for the NASH spectrum of liver disorders.

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P- 26 EFFECT OF PROTEIN X OF THE HEPATITIS B VIRUS AND HEXACHLOROBENZENE ON LIVER CELL GROWTH DYSREGULATION

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Introduction and Objectives: Chronic hepatitis B and exposure to persistent organic pollutants (COPs) can lead to cellular hepatocarcinoma (HCC), the most common liver tumor. HBV DNA encodes transactivator x, HBx protein. The HBx is required to initiate and maintain HBV replication. Hexachlorobenzene (HCB), COPśmember, is a promoter of hepatic preneoplastic foci. We have shown that HCB increases in rat liver PCNA, TGF-β1, VEGF and neo-angiogenesis in vivo models. This study aimed to analyze in vitro two models of HCC generation -associated with HCB or with the expression of HBx-.

Materials and Methods: The HCB effect on cell number (BrdU incorporation by Immunohistochemistry), PCNA (Western blot), TGF-β1 (RT-PCR) was studied in vitro in: 1.1) Huh-7; 1.2) Huh-7 transfected with HBx; 2) HepG2.2.15 (stable expression HBV) and 3) EA-hy926 (endothelial cell). In these last, an inhibitor of TGF-β1-RII (SB431542) was used. In 1.2, 2 and 3 used, 5μM HCB, 24h; in 1, we performed time (30, 60, 90 and 120) and dose (0,005; 0,05; 0,5 and 5μM) curves. Evaluated: a) PCNA protein levels, b) TGF-β1 levels and positive cell number/total cell.

Results: In Huh-7, TGF-β1 increased (20%, 69% and 78%, with 0.05, 0.5 and 5μM HCB, respectively) and PCNA (45% and 60%, with 0.5 and 5 μM HCB, respectively). In Huh-7/HBx, PCNA and TGF-β1 increased by 86% and 71%, respectively. In Huh-7/HBx and 5μM HCB, PCNA increased by 120% and TGF-β1 by 91%. In HepG2.2.15 PCNA was overexpressed by 76%. In EA-hy926, PCNA 29% and TGF-β1 by 43% increased. Both effects were prevented by pre-incubating endothelial cells with the specific inhibitor of TGF-B1 RII after HCB 5μM.

Conclusions: HCB and HBx induce cell proliferation in vitro. This effect is equivalent for both agents (HCB and HBx) and is enhanced by combining them. The proliferative effect is associated with TGF-β1 increase, which mediates the proliferation generated on both HCC and endothelial cell lines. These findings could partially explain the molecular mechanism involved in human HCC cell proliferation, disease progression and neo-angiogenesis.

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P-27 CELLULAR EFFECTS OF *IN VITRO* LIPID OVERLOAD ON HEPATIC STELLATE CELLS AND HEPATOCYTES.

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