basal promoter activity and b) p53 can induce the caspase-8 promoter via an yet unknown mechanism but independently of SP1 binding.

258 IS THERE ANY LIVER ANTI-FIBROTIC EFFECT OF K-17.22? AN EXPERIMENTAL STUDY WITH IMMUNOHISTOCHEMICAL ANALYSIS IN A RAT MODEL.

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The aim of this study was to test in a liver fibrosis model a novel natural compound, which has been shown to significantly decrease GPT level in HCV-patients. 150 SD rats were allocated into 2 groups: A) fibrosis model (02ml/kg CCL4 i.p. injection twice/week); B) as A but added with K-17.22 50mg/kg (Kyotsu, Japan). At sacrificeliver samples were used for histology, hydroxyproline determinationimmuno-histochemical analysis of activated stellate cells, Northern blot analysis of Tissue Inhibitor Metallo Proteinase-1 (TIMP-1) and a2-procollagen mRNA. Blood biochemistry, Type IV collagen 7s and hyaluronic acid were measured too. While serum level of type IV collagen 7s was not affected, hyaluronic acid level increased over 20-fold in A group ($p<0.001$). However, this was completely prevented by K-17.22 ($p<0.001$ vs A) Accordingly, increased GOT, GPT, ALP and Bilirubin level ($p<0.001$ vs healthy control) significantly improved in B group ($p<0.05$ vs A). Group A showed an increased hydroxyproline content (1190± 205 vs 343±61, $p<0.001$ vs control) which was significantly reduced by the supplementation with K-17.22 ($p<0.05$ vs A). Histolology of liver in A group showed the typical ongoing fibrosing features while an overt reduction of the above morphological abnormalities appeared in group B. K-17.22 significantly decreased the number of activated stellate cells and the expression and densitometric assessement of either TIMP-1 and a2-procollagen mRNA ($p<0.05$). These data suggest that the present novel phytotherapeutic compound K-17.22 exerts a potent antifibrotic effect and further studies are awaited to corroborate its clinical potential.

259 METADOXINE PARTIALLY PREVENTS FIBROSIS AND COMPLETELY PRESERVES GLYCOGEN STORES IN PROLONGED BILIARY OBSTRUCTION IN THE RAT: A COMPARISON WITH COLCHICINE

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Background/Aims: Metadoxine (pyridoxol l,2 pyrrolidone-5-carboxilate) is a combination of pyridoxine and pyrrolidone carboxylate. Metadoxine accelerates the plasma clearance of ethanol and acetaldehyde and has also shown antifibrotic effects in the CCl4-chronic administration model of fibrosis. To evaluate liver beneficial properties of metadoxine, not related with alcohol metabolism, bioactivation of external toxins or antioxidant mechanisms, the chronic bile duct ligation (BDL) model was used and results were compared with colchicine, a well known antifibrotic drug.
Methods: Seven groups (n=6) of male Wistar rats were performed, four groups were BDL and received metadoxine (60 mg/kg/12 hrs i.p.), colchicine (10μg/rat/day/p.o.), both, or vehicles; three groups were sham-appropriate controls. Collagen content was determined by measuring hydroxyproline in liver samples; malondialdehyde (MDA) was used to estimate lipid peroxidation levels; glycogen was determined utilizing the anthrone reagent; Gomory's trichromic stains of liver sections were performed.
Results: Collagen increased 4-fold by BDL; metadoxine, colchicine or both prevented fibrosis partially ($p<0.05$). MDA levels increased 3-fold by BDL ($p<0.05$) and no treatment had any significant effect. Glycogen was almost depleted in the cirrhotic group, metadoxine preserved glycogen completely. Bilirubins and, alanine aminotransferase and γ-glutamyltranspeptidase activities, increased several-fold in the BDL-group ($p<0.05$); both drugs prevented partially these effects ($p<0.05$). The histopathological analysis correlated with biochemical data.
Conclusions: Both compounds showed similar antifibrotic properties, but metadoxine was more effective in preserving glycogen. Besides its antioxidant effects and its ability to induce alcohol metabolism, reported by others, metadoxine possesses important antifibrotic and antinecrotic properties, and maintains energy stores efficiently.

260 SUPPRESSION OF TRANSFORMING GROWTH FACTOR-β EFFECTS UP-REGULATES EXPRESSION OF REGENERATION FACTORS IN LIVER CIRRHOSIS

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Aim: We investigated the relationship between liver regeneration mechanism and regeneration factors after anti-TGF-β molecular intervention in dimethylnitrosamine (DMN) -treated cirrhotic model rats.
Methods: Rats were first treated with DMN for 3 weeks, then intravenously injected once with AdTβ-TR (an adenovirus expressing a dominant-negative TGF-β receptor), AdLacZ (a control adenovirus expressing bacterial β-galactosidase), or saline. Following these gene transfers, the rats were not given DMN for an additional 1 week. Serial changes in hepatocyte proliferation were evaluated by immunohistochemistry using anti-Ki67 antibody. The mRNA expression of regeneration factors such as hepatocyte growth factor (HGF), HGF receptor (c-Met), transforming growth factor-α (TGF-α), epithelial growth factor (EGF) and insulin-like growth factor-1 (IGF-1) in the whole liver were evaluated RT-PCR.
Results: Hepatocyte proliferation rate peaked 3 days after anti-TGF-β molecular intervention. In AdTβ-TR-treated groups, EGF and IGF-1 mRNA expressions had already significantly increased at 2 days after anti-TGF-β molecular intervention compared with those before the transfection, and these mRNAs 5 to 7 days after anti-TGF-β molecular intervention significantly increased compared with those in AdLacZ-treated rats. TGF-α mRNA expression had increased more later than that of other regeneration factors. TGF-α mRNA expression 5 to 7 days after anti-TGF-β molecular intervention significantly increased compared with that before its transfection. HGF mRNA expression had not significantly up-regulated for 1 week after anti-TGF-β molecular intervention, whereas c-Met mRNA expression had significantly increased 3 to 7 days after anti-TGF-β molecular intervention compared with that before anti-TGF-β molecular intervention.
Conclusions: Liver regeneration after anti-TGF-β molecular intervention in DMN-treated cirrhotic model rats is suggested to be deeply involved in the expression of regeneration factors, such as EGF, IGF-1, TGF-α and c-Met.

261 DIFFERENTIAL GENE EXPRESSION PROFILE IN BUDD-CHIARI SYNDROME AND CIRRHOSIS

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Budd-Chiari syndrome (BCS) induces necrosis, regeneration, and fibrosis without chronic inflammation. To gain further insights into the pathogenesis of liver injury, we investigated whether the expression of a set of genes known to be involved in chronic inflammatory liver diseases differs in BCS livers.
Materials and Methods: Using real-time RT-PCR, mRNA expression of 35 genes involved in extracellular matrix regulation, growth factors and angiogenesis was quantified in liver explants from patients with BCS (5