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Hepatology Highlights

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Dipeptidyl Peptidase IV (DDP IV) in NASH Patients

Nonalcoholic steatohepatitis (NASH), a potential cause of end-stage liver disease and hepatocellular carcinoma, is characterized by fatty infiltration of the liver, inflammation, hepatocellular damage and fibrosis. Although in the last 5 years considerable progress has been made in the understanding of the molecular and cellular mechanisms implicated in the pathogenesis of NASH, the inner events at the basis of the accumulation of triglycerides in the hepatocytes is still not fully clarified. Comprehension of the basic mechanisms of NASH development is critical to design novel diagnostic and therapeutic strategies. Dipeptidyl peptidase IV (DPP IV) is a cell-surface dipeptidase that inactivates peptides by removing proline or alanine from the 2nd position of the N-terminal. By inactivating incretins DPPIV also improves insulin resistance and β cell function. In addition to the enzymatic activity, DPPIV acts as a receptor interacting with several proteins such fibronectin, collagen, chemokine receptor CXCR4, and CD45. Due to the involvement of DPPIV in glucose metabolism, DPPIV inhibitors have been shown to reduce insulin resistance in type 2 diabetes and are currently used as oral anti-diabetic agents. It was therefore rationale to test the activity of DPPIV in subject with NASH, where insulin resistance plays a major role. In a rather small, though well characterized subjects with NASH, the serum DPPIV activity was found to be slightly (30%) increased; no difference was found in urine. Interestingly, serum activity and hepatic expression correlated with the intensity of fatty infiltration and histological grading but not with the stage of NASH. The question raised by this observation is whether the increased activity/expression of DPPIV may be at the basis of NASH and therefore enzyme inhibitors may be a rationale approach in the treatment. Unfortunately the answer is still not available since DPPIV activity is consistently increased in chronic liver disease and associated to the severity of the disorders. It is therefore possible, and much plausible, that the increased activity of DPPIV is the effect rather than the cause of NASH. The inclusion of a group withy non alcoholic fatty liver disease (NAFLD) would have helped in answering this crucial question.

Hepatoprotective effect of Leucophyllum frutescens on Wistar rats intoxicated with carbon tetrachloride by Isaias Balderas-Renteria *et al*.

The use of plants extract in medicine dates back more that 5,000 years and in spite of this, the potentiality of several different plants in treating ailments is still largely unexplored. The beneficial effects are verbally passed from generation to generation and the real efficacy is misted by a mysterious aura which adds mysticism to the picture but prevents a stringent scientific approach. As in oriental medicine, Mexican tradition has plenty anecdotal reports of useful plans to treat different, almost always unrelated diseases. *Leucophyllum frutescens* is used by the populations of Northern Mexico and Southern US states to alleviate fever, cough, asthma, rheumatic pain and to treat liver disorders. Is the reported beneficial effect real or is part of the placebo effect related to ancient, mysterious traditions? The paper by the group in Nuevo Leon provides partial answer to this relevant question. Liver toxicity was fist induced in rats by the administration of CCl4, the animals were then treated with extract of *Leucophyllum frutescens* and the damage biochemically and histologically assessed. Methanol plant extract reduced the serum increment of liver enzymes and apparently fibrosis and regeneration although no real quantitative analysis was performed. In spite of being promising, as always this reports raises more questions that provide answers. One crucial question is if the dose used in rats may be applicable to human adults since the administration of 7-14 gr. per day may be complicated. The second, and more critical issue is the supposed mechanisms in reducing the damage. Understanding what is behind the effect(s) may help in targeting the treatment to specific active substances of the extract. There is no question that the plants will provide important compounds to treat several diseases but it is much better to administer a known dose of digoxin rather that an extract of *Digitalis Lanata* with unknown content of the active compound is.

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