

## 2<sup>nd</sup> International Conference on **Endocrinology**

October 20-22, 2014 DoubleTree by Hilton Hotel Chicago-North Shore, USA

## Combinations of pioglitazone with pentoxifylline or melatonin alleviate symptoms of non-alcoholic fatty liver in rats

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Insulin resistance, oxidative stress and cytokine imbalance are key pathophysiological mechanisms in non-alcoholic fatty liver disease (NAFLD). This study aimed at evaluating the effect of treatment with the insulin sensitizer, pioglitazone, the tumor necrosis factor- $\alpha$  inhibitor, pentoxifylline, and the antioxidant, melatonin and their combinations in rats with NAFLD. Rats were fed a high-fat diet (HFD) for eight weeks to induce NAFLD. For an additional eight weeks, rats were fed the HFD along with pioglitazone, pentoxifylline, melatonin alone or in combination. Liver index and insulin resistance index were calculated. Serum liver enzyme activities, total cholesterol, triglycerides and tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) were determined. Tissue triglycerides, malondialdehyde and reduced glutathione were measured and liver injury was evaluated by histopathological examination. HFD induced severe hepatic steatosis, inflammation and fibrosis. In addition, liver index, insulin resistance index, activities of liver enzymes and serum level of total cholesterol, triglycerides and TNF- $\alpha$  were elevated. This was coupled with an increase in tissue triglycerides, malondialdehyde and depletion of reduced glutathione. Pioglitazone, pentoxifylline and melatonin, alone or in combination; reduced the insulin resistance index, activities of liver enzymes, hepatic malondialdehyde and increased hepatic reduced glutathione level. Pentoxifylline led to a decrease in serum TNF- $\alpha$  level; however, pioglitazone and melatonin reduced serum total cholesterol and triglycerides. In conclusion, data in this study indicate that pentoxifylline and melatonin can be used as promising adjuvant therapies topioglitazone in the clinical management of NAFLD.

## **Biography**

El-Orabi N completed her PhD from Auburn University, Alabama, USA, and Postdoctoral studies at the Department of Anatomy, Physiology, and Pharmacology at Auburn University till September, 2007. She is working as Assistant Professor at Department of Pharmacology and Toxicology, College of Pharmacy, King Saud University in Riyadh, KSA since November, 2010 till now. She is member in ESPET since 2008, member in scientific and research committee at the Department of Pharmacology and Toxicology, College of Pharmacy, King Saud University and is serving as an editorial board member of number of reputed journals.

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