**Improvement effects of** **combined supplementation of low fructose diet with α-lipoic acid on** **Adiponectin-leptin ratio in high-fat diet-induced non-alcoholic fatty liver disease Rat model**

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**‌ Statement of Problem:** Non-alcoholic fatty liver disease (NAFLD) is one of the most common liver diseases which could lead to fibrosis and cirrhosis. Insulin resistance often associates with NAFLD and progression of it. The adiponectin/leptin ratio has been suggested as a maker of adipose tissue dysfunction and this emerging biomarker correlates with insulin resistance. Previous studies have reported that low-fructose diet and α-lipoic acid could prevent insulin resistance.

**Research Purpose:** In this study, a low fructose diet combined with α-lipoic acid was used to evaluate its effect on hepatic steatosis, insulin resistance and adiponectin/leptin ratio of NAFLD due to high fat diet in the Sprague-Dawley rats.

**Research Method:** Male rats (n=40) were divided into five group (n=8). Normal control group (NC), high fat diet group (HFD), fructose group (Fru), α-lipoic acid group (Lip) and fructose plus α-lipoic acid group (Fru+Lip). The high fat control group was orally treated with the high fat emulsion diet (HFD), fructose group orally treated with the HFD plus fructose (1g/kg), α-lipoic acid group orally treated with the HFD plus α-lipoic acid (60g/kg) and fructose plus α-lipoic acid group orally treated with the HFD plus fructose (1g/kg) combined with α-lipoic acid (60g/kg) once per day via gavage for six weeks. After this time, the rats were sacrificed. Serum and liver were collected for measurement of biochemical parameters, ELISA analyses and liver tissue staining with H&E. Adipose tissue was collected for measurement of PGC-1α gene expression by Real-time PCR.

**Results and Conclusion:** After six weeks, the plasma level of glucose, lipid profile, insulin resistance (HOMA-IR), TNF-α, leptin, hepatic content of malondialdehyde (MDA), triglyceride (TG) significantly increased (P<0/05), the plasma level of adiponectin, Adiponectin-leptin ratio, PGC-1α gene expression in adipose tissue significantly decreased (P<0/05) and hepatic steatosis was observed in HFD group compared to the NC group. In fructose group, serum glucose, insulin resistance (HOMA-IR), serum lipid profile, and hepatic malondialdehyde content significantly decreased and PGC-1α gene expression significantly increased compared to the HFD group (P<0/05). In fructose plus α-lipoic acid group, these parameters significantly decreased and Adiponectin-leptin ratio significantly increased (P<0/01) compared to the fructose group. This study showed that low fructose diet combined with α-lipoic acid has high improvement effect on Adiponectin-leptin ratio as a feature of nonalcoholic fatty liver disease (NAFLD) compared to the low fructose diet alone. On the base of this study, a low fructose diet combined with α-lipoic acid supplementation might provide a beneficial natural remedial product for improvement of NAFLD parameters.

**Keywords:** Insulin resistance, Adiponectin-leptin ratio, Non-alcoholic fatty liver disease