



## Fructose: a key player in metabolic derangement

Arianna Mazzoli

Obesity is a major public health problem that is obviously multifactorial, even if diet composition plays a major role. Fructose, present in small amount in many fruits, is now consumed by humans in large quantities due to the popularity of convenient, prepackaged foods and the consumption of soft drinks and juice beverages containing sucrose or high-fructose corn syrup (HFCS). This increased consumption of fructose in the last decades has been associated with increasing risk of obesity development and the consequent metabolic and inflammatory diseases.

During the years the main focus of my research has been evaluating the effects of a high fructose consumption, at different time points and under different conditions, on the energetic homeostasis of the whole organism in the animal model: I carried out a detailed analysis of the body composition and energy balance, as well as the functionality of the insulinemic system for blood glucose control, the plasma lipid profile and the inflammatory parameters, in order to highlight metabolic alterations induced by high levels of fructose in the diet. Liver function is particularly vulnerable to an increased fructose intake, since this organ is responsible for about 90% of the total metabolism of this sugar, that is not feedback regulated. Briefly, in the hepatocytes fructose can follow the de novo lipogenesis pathway, synthesizing triglycerides that will be incorporated in VLDL; if triglycerides levels increase it could be a chance to see an ectopic accumulation causing insulin resistance and fatty liver. Hepatic lipid synthesis implies greater circulation of the latter and this could affect other tissues such as skeletal muscle and adipose tissue, so I evaluated the effects of this dietary treatment on functional and morphological changes on these tissues, focusing my attention on the possible alteration of mitochondrial functions, since the mitochondria are the cell's energy central. Moreover, high fructose diet is associated with changes in microbiota composition that alters gut permeability by reducing expression of tight junction proteins. Finally, more recently I focused my attention on the analysis of cortex and hippocampus functionality, since has been showed that fructose intake can have a harmful effect on brain as well.

Based on my studies I can say that several and different are the consequences of high fructose diet on the maintenance of a healthy state: obesity, metabolic syndrome, NAFLD, type 2 diabetes. Understanding its metabolism may provide novel opportunities for therapeutic interventions.