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## Soybean oil attenuates the onset of non-alcoholic steatohepatitis and insulin resistance

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### Abstract

**Background and Aims:** General overnutrition, and a diet rich in fat and sugar are among the key risk factors for the development of metabolic diseases including diabetes type 2 and non-alcoholic fatty liver diseases (NAFLD). While being among the most commonly consumed oils world-wide, the effects of soybean oil on the development of metabolic diseases are yet not understood. Indeed, existing data is in part contradictory. Based on this background, the aim of the present study was to investigate the effects of soybean oil consumption on the development of non-alcoholic steatohepatitis (NASH), the more progressed stage of NAFLD, and insulin resistance.

**Methods:** Female C57BL/6J mice were fed either a liquid standard control diet (C) or a liquid fat-, fructose- and cholesterol-rich diet (FFC, 25E% butterfat, 50% (wt/wt) fructose, 0.155% (wt/wt) cholesterol) or a FFC supplemented with soybean oil (FFC + S, 21E% butterfat + 4E% soy oil), with FFC and FFC + S-fed groups being pair fed for 13 weeks to induce steatohepatitis. After 7 and 12 weeks of feeding, a glucose tolerance test was performed. Indicators of liver damage, inflammation, intestinal barrier function and markers of insulin signaling cascade were measured in intestinal, liver and muscle tissue.

**Results:** As expected FFC-fed mice developed early signs of NASH and insulin resistance. Despite similar caloric intake and body weight gain, development of NASH and insulin resistance were significantly attenuated in FFC + S-fed mice when compared to FFC-fed animals. Indeed, signs of hepatic inflammation e.g. number of inflammatory foci and neutrophils as well as activity of transaminase in plasma were almost at the level of control in FFC + S-fed mice. Prevalence of macrovesicular steatosis being the predominant type of fat accumulation found in FFC-fed animals was also markedly lower in FFC + S-fed mice. Furthermore, while in muscle and liver tissue of FFC-fed mice insulin receptors mRNA expression was significantly different from C-fed animals, insulin receptors expression in FFC + S-fed mice was almost at the level of controls. The protective effects of soybean oil supplementation on the development of metabolic alterations were associated with a protection against the induction of TLR4 mRNA expression and dependent signaling molecules in liver tissue.

**Conclusion:** Taking together, our results indicate that supplementation with soybean oil may attenuate the development of diet-induced NASH and insulin resistance in mice and that this may be related to alteration of TLR4-dependent signaling cascade in liver tissue. (Funded in parts by UFOP e.V.)

### Conflict of Interest

There is no conflict of interest