

# Endocrine activities of adipocytes extracted from subcutaneous and visceral adipose tissues of obese animals induced by high fat diet and supplemented with omega 3 fatty acid

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## Abstract

The efforts dedicated to finding the cure for obesity and associated disorders lead to an intense interest in adipocyte metabolism. The consumption of  $\omega$ -3 fatty acids (FA) presents beneficial effects on changes caused by obesity. The aim of this study was to investigate the adipokines secretion of isolated adipocytes from obese mice induced by high fat (HF) diet, supplemented or not with fish oil (FO) [rich in  $\omega$ -3 FA (EPA/DHA, 5:1)] with emphasis on the differential response of subcutaneous and visceral adipose deposits, inguinal (ING) and retroperitoneal (RP) region, respectively. C57BL/6J mice received control (CO) or HF diet for 8 weeks. Supplementation with FO (2 g/Kg p.c., 3 times/week) was initiated 8 weeks after the induction of obesity, remaining until the end, totaling 16 weeks of experimental protocol. The white adipose tissue ING and RP were removed for isolation of adipocytes that were subjected to D'MEM / 10% FBS culture for 30 hours. At the end, adipokines concentrations in the culture supernatant were determined using specific ELISA kits. The adipocytes of the HF group showed a significant hypertrophy followed by an increase in the secretion of proinflammatory cytokines TNF- $\alpha$  and IL-6 compared to the CO group, whereas the HF + FO group presented total reversion of this effect, in both ING and RP adipocytes. There was no difference in secretion of adiponectin. The relevance of isolated adipocytes in the secretion of these cytokines is highlighted here. The adipocytes are affected by the HF diet and the FO has a protective effect on these parameters.

Obesity, and health complications stemming from it, such as insulin resistance and type 2 diabetes, has become one of the main causes of mortality in developed countries. Among factors predisposing to the development of insulin resistance, environmental factors, such as the lack of physical activity (sedentary lifestyle) and an improper diet, were distinguished. It is well-established that the consumption of a high-fat diet (HFD) enriched in saturated long-chain fatty acids, as well as a Western diet rich in saturated fats and sugar, leads to the induction of insulin resistance, whereas a diet rich in polyunsaturated fatty acids (PUFA) may exert a positive influence on human health, including cardiovascular system, brain function, insulin resistance, and prevention of inflammation. It has been shown that the consumption of a Western diet, which is poor in n-3 polyunsaturated fatty acids (OMEGA-3) and rich in n-6 polyunsaturated fatty acids (OMEGA-6), leads to an increase in the n-6:n-3 ratio, to a range from 10:1 to 20:1. Another study indicated that high dietary n-6: n-3 PUFA ratio is positively associated with excessive adiposity and worse metabolic profile,

specifically regarding insulin and HOMA-IR values in the Mexican population. Overweight or obese women with polycystic ovary syndrome, who have increased consumption of only OMEGA-3 fatty acids, showed lower levels of glucose, insulin, HOMA-IR, and triglycerides (TG) as well as higher levels of adiponectin as compared to the placebo group. The decreased level of triacylglycerol (TAG) and non-esterified fatty acids was observed also in men with metabolic syndrome after the n-3 PUFA supplementation. Couet et al. indicate that dietary fish oil decreases body fat mass and stimulates lipid oxidation in healthy adults. Despite the fact that there is evidence that OMEGA-3 is beneficial, there are still some studies that speak about the unfavorable effect of PUFAs, especially when OMEGA-3 were used as the primary source of PUFAs to treat patients with type 2 diabetes. In rodents studies, accumulating evidence suggests that, in skeletal muscles, the diet enriched with OMEGA-3 PUFAs leads to improved insulin sensitivity in rats, and increased expression of genes regulating glucose metabolism and reduced biologically active lipid content in C57BL6 mice. The latest study indicates that fish oil supplementation, which includes eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), improves HFD-induced imbalance of lipid homeostasis not only in muscles but also in rat adipose tissues. Although numerous studies have highlighted the beneficial effect of dietary fish oil, especially in animals' models, the cellular and molecular mechanism, by which these beneficial actions are exerted, remains unclear. A possible explanation for the positive effect of PUFA on insulin sensitivity may be their effect on the improvement of mitochondrial function

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