Summary

(Xenobiotics in food end their effects on the human organism)

One of the exposure pathways to xenobiotics in humans is food intake. Most of xenobiotics are lipophilic substances cumulating in the organism, especially in the adipose tissue. If their intake is long-term and excessive, they have negative impact on human health. Eating habits, identification, analysis, and management of risks stemming from foods are important from a prevention perspective. The adipose tissue influences the distribution and especially accumulation of xenobiotics in the organism. Whether substances stored in the adipose tissue are able to affect adipogenesis and physiological functions, remains unclear. Since obesity-related dysfunctional and inflamed adipose tissue is associated with systemic inflammation, ectopic fat deposition, and multiorgan dysfunction, resulting in cardiometabolic complications of obesity; this knowledge would be immensely valuable.

The study focused on the basic pathophysiological mechanisms at the level of adipocytes, specifically, the study of risk and protective factors. From preventive factors, the effect of phytoprotective substances with antioxidative potential was studied. Among the risk factors, we concentrated on the impact of persistent organic pollutants (POP´s). We observed exposure to POP´s during the differentiation of mesenchymal stem cells into adipocytes, and the impact of chronic exposure on mature adipocytes.

In the model experiment of chronic exposure of adipocyte differentiating from human mesenchymal stem cell (hMSC) to 2,2-bis (4-chlorophenyl)-1,1,1-trichlorethylene (p,p´- DDE), the basic parameters such as the size and amount of lipid vacuoles in the adipocyte; transport and storage of substances in lipid vacuoles; cell metabolism via mitochondrial respiration, adenosine triphosphate or reactive oxygen species synthesis, and superoxide dismutase activity were assessed on days 0, 4, 10, and 21. We employed fluorescent probes, oil red O staining, indirect fluorescence, high resolution respirometry, measurement of citrate synthase activity, and measurement of the mitochondrial membrane potential. The statistical analysis of results was performed using MATLAB statistic Toolbox (MathWorks Inc., Natick, MA, USA), and OriginPro 2017 (OriginLab Corp., Northampton, MA, USA).

We proved different impacts on adipocyte differentiation dependent on the chronic dose of pollutant: In case of lower concentration (1 μM p, p´-DDE), we observed an increase of the MMP, an increase of the basal as well as ATP-linked mitochondrial respiration, indicating obesogenic potential by means of decrease of heat production, higher proliferation, and viability of adipocytes. The higher concentration (10 μM p, p´-DDE) slowed down the differentiation process. These experiments demonstrated the potential of p, p´-DDE exposure to interfere with physiological adipogenesis, and metabolic programming of mature adipocytes, in a dose-dependent manner.

Keywords: xenobiotics, adipose tissue, persistent organic pollutants