

**Modulation of adipocytes differentiation and proadipogenic genes expression by different bioactives**

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Obesity, considered as one of the most easy to recognize but most difficult to treat medical conditions, is the main dysfunction of adipose tissue. It is characterized by excess body fat accumulation due to an increase in size and number of differentiated mature adipocytes. De novo generation of fat cells plays a key role in the development of obesity and adipocytes differentiation is a complex process involving the coordinated interplay of numerous transcriptional regulators and genes. Discovering natural compounds able to regulate size, number and function of adipocytes could greatly contribute to obesity prevention and treatment; particularly natural compounds could represent a potential novel strategy already exploited for preventing metabolic disorders. The current study had two aims: (1) to evaluate changes in the expression of adipogenic markers at four stages of the differentiation process; and (2) to investigate the anti-obesity effectiveness of the anti-adipogenic ability of three bioactives, docosahexaenoic acid (DHA), genistein (GEN), and sulforaphane (SFN). Using murine 3T3-L1 pre-adipocytes changes in the expression of adipocyte marker genes C/EBP $\alpha$ , PPAR $\gamma$  variant1 and variant 2, and GLUT 4 at growing, postconfluent, differentiating and mature adipocyte cell stages were evaluated by RT-qPCR. The ability of SFN, GEN and DHA to inhibit 3T3-L1 differentiation was assessed by both lipid accumulation and modulation of the above mentioned genes expression in mature adipocytes. Expression of the four marker genes was low and similar at the early stages of pre-adipocytes development, whereas a prominent increase was observed in mature adipocytes. The bioactive compounds were shown to suppress adipocytes differentiation and to decrease the expression of the adipogenic markers and lipid accumulation to the levels of pre-adipocytes. These results set the stage for further studies considering natural food constituents as important tools in preventing or treating obesity. The authors participate in the FP7 EU Project PATHWAY-27 'Pivotal Assessment of the Effects of Bioactives on the Health and Wellbeing, from Human Genome to Food Industry' (grant agreement no. 311876).



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