

EFFECT OF A FLAVONOID-RICH EXTRACT OF ORANGE JUICE ON WEIGHT MANAGEMENT IN AN *IN VIVO* MODEL OF OBESE ZEBRAFISH

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Introduction: Obesity is a pathological condition due to an imbalance between energy intake and its expenditure, that has reached epidemic proportions. Therefore, the efforts of the scientific community are focused on finding novel strategies to prevent obesity and new effective treatments to reduce it. Recently, we witnessed a sharp increase in the interest on plant derivatives, thanks to their potential health-promoting properties, such as the anti-obesity one. Orange (*Citrus sinensis*) juice (OJ) exerts different beneficial effects, among which a possible role in weight management. The present study was designed to evaluate the effect of a flavonoid-rich extract of OJ (OJe) in diet-induced obese zebrafish, an *in vivo* model structurally and functionally like humans.

Materials and methods: Adult zebrafish were divided into four diet groups (n=15each): i) normal fed (NF) receiving a diet containing 20 mg of *Artemia nauplii*; ii) overfed (OF) receiving a diet containing 60 mg of *Artemia nauplii*; iii) NF supplemented with OJe (5ml/l in fish water); iv) OF supplemented with OJe (OF + OJe). Treatments lasted five weeks. Each week, body weight (BW) and length were measured to evaluate differences in body mass index (BMI). At the end of the treatments, zebrafish were euthanized and processed for the extraction of RNA for quantitative real-time PCR or fixed for microscopical evaluations.

Results: As expected, OF zebrafish exhibited a significant increase in both BW and BMI compared to NF ($p < 0.001$), while, the supplementation with OJe significantly decreased both values only in OF, already at the second week. OJe significantly lowered also visceral adipose tissue in OF zebrafish ($P < 0.001$), with little effect on NF one. Moreover, OJe significantly reduced adipocyte cell size in both NF and OF groups in both visceral and subcutaneous adipose tissues, as well as their number in OF fish ($p < 0.001$). Finally, the abovementioned effects were coupled to a modulation of appetite-related genes such as leptin, ghrelin, orexin, pro-opiomelanocortin and neuropeptide Y, in both gut and brain.

Discussion and conclusion: This study adds new insights into the anti-obesity property of OJ and its flavonoids, suggesting their role as weight management agent, through a lipolytic action linked to a restoration of the appetite-regulating genes expression.