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## Evolution of plasma inflammatory biomarkers after the intake of an orange-based beverage enriched with polyphenols in overweight adults (BIONAOS Study)

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The prevalence of obesity is continuing rising. A large body of evidence clearly suggests that obesity is associated with a chronic pro-inflammatory state. Chronic inflammation may contribute to insulin resistance, metabolic syndrome (MS) and atherosclerosis. It seems that some food components may help to the prevention of metabolic disorders and inflammatory complications. The aim of the present work is to evaluate the evolution of plasma inflammatory biomarkers after the intake of a polyphenol-enriched orange juice in overweight adults.

A total of 150 volunteers (age 18–65 y) were included in a randomized, placebo-controlled, double-blind, crossover trial. Among them 45 were overweight (BMI 25–30 kg/m<sup>2</sup>), 60 obese (BMI 30–40 kg/m<sup>2</sup>) without MS and 45 obese with MS. Volunteers were randomly assigned into two groups. One group consumed 2 daily doses (250 ml each) of an orange juice enriched in polyphenols (582.5 mg of hesperidin, 125 mg of narirutin and 34 mg of didymin, daily) during 12 weeks, and following a 8-week wash out period, they consumed 2 daily doses (250 ml each) of an orange juice with lower levels of polyphenol (237 mg of hesperidin, 45 mg of narirutin and 17 of didymin, daily) during 12 weeks. The second group started with the reference juice in the first 12-weeks period and took the polyphenol-enriched juice in the second period after the wash out. Here, we are presenting results from the subsample of 45 overweight volunteers. Plasma inflammatory biomarkers were measured in fasting blood samples at baseline, 12, 20 and 32 weeks by using a Human Adipokine Panel B kit (LINCoplex™) with the Luminex 200 System built on xMAP technology. The determination of hesperetin, naringenin and their metabolites were carried out using a UHPLC system (1290 Infinity series, Agilent Technologies) equipped with a triple quadrupole mass spectrometer (6460 series, Agilent Technologies) (UPLC-MS/MS). Differences between groups were evaluated by using the General Linear Model for covariance (ANCOVA) adjusted by initial time. Correlations between parameters were estimated by computing Pearson's correlation coefficient.  $P < 0.05$  were considered to be statistically significant between groups and is indicated with \*. All statistical analyses were performed with the SPSS 15.0 for Windows.

	Orange juice enriched in polyphenols				Reference				P values
	Initial		Final		Initial		Final		
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	
IL-1 $\beta$ (pg/ml)	0.95	0.16	0.49	0.04	0.48	0.05	0.51	0.05	0.659
IL-6 (pg/ml)*	5.11	0.51	3.27	0.23	3.24	0.24	3.52	0.20	0.015
IL-8 (pg/ml)*	2.21	0.17	1.43	0.10	1.52	0.12	1.48	0.10	0.045
MCP1 (pg/ml)	15.45	0.88	12.97	0.58	12.84	1.47	13.14	0.51	0.059

A significant higher urinary excretion was found after the ingestion of the polyphenol-enriched orange juice during 12 weeks. Indeed, levels of urinary hesperetin and plasma IL-6 were significantly correlated ( $r = -0.147$ ,  $P = 0.019$ ). Therefore, the enrichment of an orange juice with flavanones, mainly hesperidin, decreased pro-inflammatory biomarkers, IL-6 and IL-8, what may be useful in the prevention of the inflammatory complications of obesity.

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