Identification of molecular targets of hesperidin, major polyphenol of the orange juice, in relation with its beneficial vascular action in healthy men

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Epidemiological and clinical studies suggest beneficial effects of dietary polyphenols, natural antioxidants present in fruits and vegetables, against cardiovascular disease (CVD) development (Arts et al., 2005; Minks et al., 2007; Hooper et al., 2008). There is growing evidence that these protective effects could be independent of their capacity to inhibit lipid peroxidation and LDL oxidation (Manach et al., 2005), but rather mediated by changes in gene expression, which mechanisms remain still widely unknown (Auclair et al., 2009).

The goal of this study is to identify the effects of hesperidin, the major polyphenol of oranges, on vascular function and gene expression in human leukocytes, that may reflect systemic effects in CVD

Study design and methods

- 24 healthy male subjects
- Inclusion criteria: i) 50-65 yrs old; ii) BMI >25 kg/m²

Inclusion

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<th>B</th>
<th>C</th>
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<td>1 week</td>
<td>A, B or C</td>
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<td>3 weeks</td>
<td>A, B or C</td>
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<td>Overnight fast</td>
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<td>Day 0</td>
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<td>4 weeks</td>
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<td>Day 28</td>
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- A: 500 ml/d of orange juice
- B: 500 ml/d of an isocaloric control drink + 1 placebo capsule
- C: 500 ml/d of an isocaloric control drink + 1 capsule filled with 292 mg Hesperidin (equals to that brought by the orange juice)

BS (Blood Sampling) - determination of systemic parameters related to CVD risk, including sVCAM-1, NO pool (nitrite + nitrates) - transcriptomic study on leukocytes

VRM: Vascular Reactivity Measurement / BP: Blood Pressure

Blood pressure measurement

Measurements were performed in a seated position after a 15 min rest before recording. Three readings, taken at 5 min intervals, were averaged.

Statistics

Analyses were performed using SAS software. The baseline-adjusted between group differences were analyzed with random effect models using a PROC MIXED GLM procedure (SAS), with Tukey’s adjustment for multiple comparisons.

Results

Functional & Systemic measurements

- Diastolic blood pressure
- Microvascular endothelial response
- Plasma NO pool
- Plasma sVCAM-1

Leukocytes Microarray analysis

Microarray analysis performed on leukocytes revealed that 1,582 genes are differentially expressed by both, orange juice and hesperidin consumption. Most of these genes are involved in biological functions implicated in CVD development, such as lipid transport, chemotaxis, cell adhesion and trans-endothelial migration.

Conclusion

This study revealed that a 1 month regular consumption of orange juice improves the diastolic component of blood pressure, an indicator of vessel resistance, and this effect is mimicked by hesperidin. The high homology between the leukocyte transcriptomic profiles after consumption of orange juice and pure hesperidin, indicates that hesperidin is highly involved in the genomic effects of orange juice.

The analysis of the modulated genes suggests that the molecular targets of hesperidin are associated with processes involved in the control of CVD development and thus may contribute to the vascular health effects of orange juice.

References


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ALIMENTATION

AGRICULTURE

ENVIRONNEMENT