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NUT CONSUMPTION REDUCES INFLAMMATION, A MECHANISM IMPLICATED IN DIABETES, ATHEROSCLEROSIS AND OTHER CHRONIC DISEASES

Nut consumption has been associated with an anti-inflammatory effect potentially explaining the beneficial effects on cardiovascular disease prevention. The anti-inflammatory effect of nuts may also contribute to prevent other chronic diseases such as type 2 diabetes, dyslipidemia, metabolic syndrome and cognitive decline associated to aging.

he benefits of nut consumption on cardiovascular health have been consistently supported by several evidences. Several epidemiologic studies have shown an inverse association between the frequency of nut consumption and the risk of cardiovascular disease (CVD) and type 2 diabetes (T2D)¹, which share a low-grade systemic inflammation as a well-established common antecedent².

Nuts, a key component of the Mediterranean Diet (MedDiet), may confer protection against inflammation due to their content in a variety of healthful components such as magnesium, fiber, α -linolenic acid, L-arginine, antioxidants and unsaturated fatty acids³. Therefore, many studies^{4,5} have evaluated the effect of nut consumption in different inflammatory biomarkers.

"The anti-inflammatory effect could be explained by the variety of healthful components in nuts, such as magnesium, fiber, α-linolenic acid, L-arginine, antioxidants and unsaturated fatty acids.

Different epidemiologic studies have demonstrated an inverse association between nut consumption and inflammation. In 2008, the Primary Prevention of Cardiovascular Disease with a Mediterranean Diet (PREDIMED) study⁴ showed that those individuals who had the highest nut intake at baseline, presented lower concentrations of some peripheral inflammatory biomarkers; such as interleukine-6 (IL-6), intracellular adhesion molecule-1 (ICAM-1), and the C-reactive protein (CRP) which is the end product of the in vivo inflammatory cascade in our bodies. Furthermore, a sub-analysis of the Multi Ethnic Study of Atherosclerosis⁵ concluded that a frequent consumption of nuts was associated with lower concentrations of CRP, IL-6 and fibrinogen.

On the other hand, a recent cross-sectional study⁶ published by the Harvard T.H Chan School of Public Health has focused on assessing the associations between nut consumption and some fasting plasma inflammatory biomarkers in 5013 non-diabetic participants, from 2 large prospective cohorts: The Nurses' Health Study (NHS) and The Health Professionals Follow-Up Study (HPFS).

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In this paper, researchers showed that a higher consumption of nuts (peanuts + other nuts) was associated with lower amounts of some plasma inflammatory biomarkers such as CRP and IL-6 after adjusting for demographic, medical, dietary, lifestyle and other confounding variables. This association comparing subjects with nut intake of \geq 5 times/wk and those in the categories of never or almost never consuming was independent of body mass index and did not differ by sex. In addition, higher consumption of other types of nuts was significantly associated with lower concentrations of some inflammatory molecules in blood, such as CRP and IL-6, whereas a high consumption of peanuts was associated with lower levels of CRP and Tumor Necrosis Factor 2.

Furthermore, these researchers also assessed the effect of substituting 3 servings of nuts/wk for 3 servings of red meat, processed meat, eggs or refined grains/wk and this theoretically substitution was associated with significant lower peripheral levels of CRP and IL-6. Similarly, CRP also was lower when substituting 3 servings of nuts/wk for potatoes and potato chips.

Some clinical trials have also demonstrated the anti-inflammatory effect of nuts. The results of one of these trials deserve to be highlighted: the PREDIMED study. This study⁷ is a parallel-group, singleblind, multicenter, randomized, controlled clinical trial conducted in Spain evaluating the effects of the MedDiet in the context of primary prevention of CVD. A recent scientific paper⁸ reported the long-term antiinflammatory effects of a MedDiet supplemented with extra-virgin olive oil (EVOO) (1 L/wk for the participants and their families) or nuts (15 g walnuts, 7,5 g almonds and 7,5 g hazelnuts).

In this study, Casas and collaborators⁸ evaluated changes in the expression of adhesion molecules related to atheroma plaque formation and changes in the plasma concentrations of the main immunomodulatory biomarkers [high-sensitivity C-reactive protein (hs-CRP), IL-6, tumor necrosis α (TNF- α) and monocyte chemoattractant protein 1 (MCP-1)] in relation to atherosclerosis after 3 and 5 years of intervention in a subcohort of the PREDIMED study⁷. A total of 165 participants at high cardiovascular risk were randomly assigned to one of the 3 intervention groups [MedDiet supplemented with EVOO, MedDiet supplemented with mixed nuts, or advice to follow a low-fat diet (LFD)].

The main changes observed at 3 and 5 y were the down-regulation of different clusters of differentiation (CD), which are surface molecules that play a role in cell adhesion (important molecules implicated in the process of atherosclerosis plaque formation) in the 3 intervention groups. Furthermore, CD49d and CD40 expression in peripheral T lymphocytes was down-regulated in both MedDiet groups, whereas CD49d expression was increased in the control group. In the LFD group, CD40 was also incremented at 5 y. Similarly, CD11b, CD49d and CD40 were significantly decreased in circulating monocytes in the 2 MedDiet groups after the intervention at 3 and 5 y.

After comparing the 3 intervention groups, a greater reduction of CD49d and CD40 expression in T lymphocytes was observed in both MedDiet groups than in the LFD group. Regarding monocytes, a higher reduction was observed in CD11b expression in the MedDiet+nuts group after 5 years, and a lower expression of CD49d and CD40 in the 2 MedDiet groups than in the LFD group. Importantly, both MedDiet groups

had significant reductions in plasma concentration of inflammation biomarkers such as hs-CRP, IL-6, TNF- α and MCP-1 at 3 and 5 y. However, after comparing the 3 intervention groups, the MedDiet+nuts group only had a significant reduction in MCP-1 and IL-6 compared with the control group. Therefore, this study reinforces the notion that nut consumption has beneficial effects on inflammation, a mechanism implicated in diabetes, atherosclerosis and other chronic diseases.

To conclude, nut consumption has consistently shown to lower plasma inflammatory biomarkers, and this anti-inflammatory effect on cardiovascular health may be sustained in the long term. In addition, the anti-inflammatory effect of nuts may contribute to prevent chronic diseases such as T2D and CVD, as it has been documented by several epidemiologic studies. Moreover, the substitution of nuts for other "unhealthy foods" such as red and processed meat, refined grains, potatoes or potato chips has been related with a healthier inflammatory profile[6].

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