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DIABETES

Oxidative Stress and Dietary Antioxidants

SECOND EDITION

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CHAPTER 32

Salvia hispanica L. and its therapeutic role in a model of insulin resistance

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Abstract

Obesity and particularly visceral adiposity are accompanied by and increased oxidative stress (OS) due to unfavorable critical balance between free radicals generation and antioxidant defenses that in turn affect insulin signaling and contribute to insulin resistance. All of them key factor of the metabolic Syndrome. Recent investigations showed that increases consumption of natural dietary sources with antioxidant bioactive compounds may support the prevention of OS. *Salvia hispanica* L seed is a richest botanical source of α-linolenic acid 18:3 n-3 and is a promising source of antioxidants, because it contained considerable amount of chlorogenic and caffeic acids, myricetin, quercetin, kaempferol, among others. This chapter analyzes the effect of dietary Salvia *hispanica* L seeds upon the improvement and /or reversion of OS and its

relationship with insulin insensitivity, mainly focuses in the adipose tissue of an experimental model of dyslipidemia, impaired glucose homeostasis, insulin resistance and visceral adiposity.

Introduction

Today, there is increasing interest in the role of dietary polyunsaturated n_3 fatty acids (n_3 PUFAs)—EPA (eicosapentaenoic acid 20:5 n_3), DHA (docosahexaenoic acid 22:5 n_3), and ALA (α-linolenic acid 18:3 n_3) from marine or plant origins—in the prevention or progression of dyslipidemia, hypertension, altered glucose tolerance, obesity, insulin resistance(IR), visceral adiposity, and systemic oxidative stress(OS) among others, all of them key components of the metabolic syndrome (MS). This syndrome increases the risk of type 2 diabetes and cardiovascular disease and is today considered as one of the important health problems in both the developed and undeveloped countries.[1_3] In modern societies, obesity and particularly visceral adiposity have been related to excessive food ingestion and increased consumption of diets rich in high saturated fat, sucrose, or fructose.[4] The hypertrophied visceral adipose tissue is accompanied by a low-grade chronic inflammation and increased OS, due to an unfavorable critical balance between free radical generation and antioxidant defenses that in turn affect insulin signaling and nitric oxide availability and contribute to IR. Additionally, adipocyte hypertrophy in visceral but not subcutaneous fat is associated with the metabolic perturbation of lipidmetabolism.[5,6]

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ORIGINAL CONTRIBUTION

Dietary Salba (*Salvia hispanica* L.) ameliorates the adipose tissue dysfunction of dyslipemic insulin-resistant rats through mechanisms involving oxidative stress, inflammatory cytokines and peroxisome proliferator-activated receptor γ

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Abstract
Purpose Rats fed a long-term sucrose-rich diet (SRD) developed adipose tissue dysfunction. In the adipose tissue of these SRD-fed rats, the present study analyzed the possible beneficial effects of dietary Salba (chia) seeds in improving or reversing the depletion of antioxidant defenses, changes in pro-inflammatory cytokines and ROS production.
Methods Wistar rats were fed a SRD for 3 months. After that, half of the animals continued with the SRD until month 6, while in the other half, corn oil was replaced by chia seeds for 3 months (SRD + chia). A reference group consumed a control diet all the time.
Results Compared with the SRD-fed rats, the animals fed a SRD + chia showed a reduction in epididymal fat pad weight; the activities of antioxidant enzymes CAT, SOD and GPx returned to control values, while GR significantly improved; mRNA GPx increased, and both mRNA SOD and the redox state of glutathione returned to control values; a significant increase in the expression of Nrf2 was recorded. These results were accompanied by a decrease in XO activity and ROS contents as well as plasma IL-6 and TNF-α levels. Chia seeds reversed the decrease in PPARγ protein mass level and increased the *n-3/n-6* fatty acids ratio of membrane phospholipids. Besides, dyslipidemia and insulin sensitivity were normalized.
Conclusion This study provides new information concerning some mechanisms related to the beneficial effects of dietary chia seeds in reversing adipose tissue oxidative stress and improving the adipose tissue dysfunction induced by a SRD.

Keywords α-linolenic acid (ALA) · Adipose tissue · Dyslipidemia · High-sucrose diet · Oxidative stress · Insulin resistance

Introduction

Excessive food ingestion and the increase in the consumption of high-fat, fructose or sucrose diets characteristic of modern society have been related to the development of visceral adiposity, systemic oxidative stress, impaired glucose homeostasis, insulin resistance (IR), type 2 diabetes, dyslipidemia and hypertension, the major components of the metabolic syndrome (MS) [1, 2]. Experimentally, our group and others have demonstrated that rats chronically fed a sucrose-/fructose-rich diet develop metabolic and physiological alterations mimicking several aspects of the metabolic syndrome in humans [3–5].

Diets can play a major role in the prevention or improvement in this syndrome and its associated pathologies. In addition to other lifestyle interventions, it has been recognized that adjustments to the quality of dietary lipids such as *n-3* polyunsaturated fatty acids (*n-3* PUFAs) from marine [fish oil; eicosapentaenoic acid (EPA) 20:5, *n-3*; docosahexaenoic acid (DHA) 22:6, *n-3*] or plant sources

M. R. Ferreira and S. M. Alvarez have contributed equally to the laboratory assays in the present study.

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Dietary Salvia hispanica L. reduces cardiac oxidative stress of dyslipemic insulin-resistant rats

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ABSTRACT

Salvia hispanica L., commonly known as chia seed, has beneficial effects upon some signs of metabolic syndrome (MS), such as dyslipidemia and insulin resistance. However, its action on cardiac oxidative stress associated with MS remains unknown. The goal of this study was to analyze the possible beneficial effects of chia seed (variety Salba) upon the oxidative stress of left ventricle heart muscle (LV) of a well established dyslipidemic insulin-resistant rat model induced by feeding them a sucrose-rich diet (SRD). Male Wistar rats received an SRD for three months. After that, for three additional months, half of the animals continued with the SRD, while the other half received the SRD containing chia as the source of dietary fat instead corn oil (SRD+chia). In the LV of SRD-fed rats, chia seed improved/reverted the depleted activity of antioxidant enzymes glutathione peroxidase, superoxide dismutase (SOD), and catalase, and ameliorated MnSOD mRNA levels increasing the expression of the nuclear factor Nrf2. Improved the glutathione redox estate, reactive oxygen species, and TBARS contents normalizing the p47NOX subunit mRNA level. Furthermore, chia normalized hypertension and plasma levels of pro-inflammatory cytokines and oxidative stress biomarkers. The findings show that chia seed intake impacts positively upon oxidative unbalance of LV of dyslipidemic insulin-resistant rats. Bullet points: ●Healthy effects of chia seed involve an improvement of cardiac antioxidant defenses through Nrf2 induction. ●Chia seed intake reduces cardiac oxidative stress markers of dyslipemic insulin-resistant rats. ●Dietary chia seed restores cardiac unbalanced redox state of dyslipemic insulin-resistant rats.