Justo Javier Pedroche Jiménez
Francisco Millán Rodríguez
(coords.)

CHÍA

(Salvia hispanica L.)

THE OLD FOOD OF THE FUTURE (CIRCHIA2016)

CHIA LINK
Red internacional

Based on presentations made at the II International Conference of the Chía-Link Network held at the Instituto de la Grasa from october 5 to 7, 2016

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RESEÑA ››

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IMMUNONUTRITIONAL INFLUENCE OF CHIA ON THE HEPATIC METABOLIC DYSFUNCTION

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SUMMARY: The study approaches immunonutritional effects of a chia-containing (*Salvia hispanica* L., 5%) bread formulation (ChB) on biomarkers that are important determinants of intestinal and liver metabolic health. ChB was compared to whole wheat and white bread in relation to the glycaemic index, and the hepatic expression of transferrin receptor 2 (TfR2) as systemic iron sensor and peroxisome proliferator-activated receptor gamma (PPARγ) as key regulator of nutrients distribution. Chia flour as breadmaking ingredient promoted beneficial changes in immunonutritional biomarkers with potential relevant implications for insulin resistance and an inflammatory state.

Keywords: Chia bread, glycaemic index, PPARγ.

RESUMEN: *Influencia inmunonutricional de la chía en la disfunción metabólica hepática.* El estudio evalúa la influencia de una formulación panaria con chía sobre parámetros inmunonutricionales importantes para la salud intestinal y metabolismo hepático. La formulación panaria con harina de chía (*Salvia hispanica* L., 5%) se comparó con panes de trigo integral y blanco en relación al índice glucémico y la expresión hepática del receptor de transferrina 2 debido a su papel como sensor sistémico de hierro y de PPARγ como regulador crítico de la distribución metabólica de nutrientes. La inclusión de harina de chía como nuevo ingrediente en panificación favoreció variaciones beneficiosas

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en los biomarcadores inmunonutricionales con una potencial implicación relevante en la prevención de la resistencia a insulina y un estado inflamatorio.

Palabras clave: Pan con chía, índice glucémico, PPARγ.

1. INTRODUCTION

Western diet commonly favors overnutrition with an altered food supply and a particular high intake, among others, of refined grains. Type and amount of dietary carbohydrates are important determinants of postprandial glucose and insulin responses. Currently, it has been demonstrated that high-glycaemic index (GI) diets are associated with developing metabolic dysfunction and predispose to type 2 diabetes (T2D) and overweight/obesity and associated risk factors in children and adolescents.

To tackle this worldwide spread pandemic several different immunonutritional strategies are currently being used. In this context, clarification of the influence of innovative bread formulations is needed to facilitate the development of effective nutritional intervention strategies.

2. MATERIALS AND METHODS

2.1. Breadmaking

Compressed yeast (*Saccharomyces cerevisiae*) was used as a starter in identical breadmaking processes to prepare chia-containing bread formulation at 5% according to previously established processes (Iglesias-Puig &Haros, 2013).

2.2. Animals

For the experiments there were used Wistar rats in strict accordance with the recommendations included in the Guide for the Care and Use of Laboratory Animals of University of Valencia (SCSIE, University of Valencia, Spain).

2.3. Glucose quantification

Blood glucose was determined using a commercial glucometer (Accu-Chek®, Roche). The data obtained were used to plot time-course curves to calculate the area under the curve (AUC) for each treatment group (SigmaPlot

v10.0, Systat Soft. Inc, UK). From the AUC values there were calculated apparent hydrolysis indexes (HI) in relation to a reference sample (white bread) as HI (%) = ($AUC_{Bread\ formulation}/AUC_{White\ bread}$) x 100. The estimated glycemic indexes (GI) were calculated as previously described (GI = 39.71 + 0.549 (HI)) (Mardiana & Noor, 2009).

2.4. Hematological parameters

Hemoglobin (Hb) concentration was determined according to the International Council for Standardization in Hematology (ICSH) (Laparra *et al.*, 2014).

2.5. Gene expression of hepatic biomarkers

Total RNA was extracted from liver tissue samples using an RNeasy mini kit (Qiagen, USA) and the transcripts of TfR2, PPARγ and β-actin, used as a housekeeping gene, were analyzed by reverse transcription-real time PCR (Laparra *et al.*, 2014).

2.6. Statistical analysis

The analyses were performed using SPSS v.15 software (SPSS Inc., Chicago, IL, USA) and statistical significance was established at $P<0.05$ for all comparisons.

3. RESULTS

3.1. Glycaemic index

Time course of glucose concentration in animals fed with the different bread formulations is shown in Fig. 1. Overall, maximum glucose concentrations were quantified after 20 min as follows: ChB < WWB < WB. The slopes that can be calculated from plotting blood glucose concentrations during this period of time reveal different kinetics for glucose absorption that result clearly advantageous when feeding ChB in comparison to WB.

The AUC values, HI and estimated GI for the different bread formulations are shown in Fig. 2. Feeding WWB or ChB significantly decreased ($P<0.05$) AUC values in relation to WB. Notably, HI values calculated for WWB and ChB were about 10.3% and 31.1% lower than values calculated for WB, respectively.

Significant decreases of HI values in bread samples were reflected in significantly ($P< 0.05$) decreased GI values.

3.2. Hepatic biomarkers

Changes in the gene expression (mRNA) of TfR2 and PPARγ in animals fed with the different bread formulations are shown in Fig. 3. Only ChB had a significant influence on Fe bioavailability at the investigated level of substitution that was reflected in a down-regulated expression of TfR2. There were quantified changes in the expression of PPARγ according to the following gradation: ChB > WWB = WB.

4. DISCUSSION

Several different technological factors have been shown to influence GI of food, but also the effect attributable to other ingredients is of physiological relevance. Notably, differences in lipid profiles and their associations with glycemic outcomes have been identified in obese, nondiabetic patients during weight-management interventions (Valsesia *et al*., 2016). An aim of weight loss is to reduce the risk of T2D; however, the relation of lipid metabolism and long-term effects on glucose homeostasis remains unsolved. In this context, prior research has largely focused on total calorie intake and consumption, with a continuous positive balance promoting obesity and/or the metabolic syndrome and finally fatty liver. Recent data suggest that the composition of the food, irrespective of calorie count, and its influence on and interaction with the gut microbiota, and finally their crosstalk with the host's intestinal immune system may be even more important determinants of liver metabolic health.

Impaired glucose tolerance is accompanied by increased measures of oxidative stress as well as increased systemic iron (i.e., serum ferritin) because the decreased iron transport due to impaired insulin signalling. Ferritin is found in most tissues as a cytosolic protein, but small amounts are secreted into the serum where it functions as an iron carrier. Importantly, this alteration on iron status appears associated to the metabolic syndrome and progression of non-alcoholic fatty liver disease (Jin *et al*., 2015). Moreover, there is increasing evidence from mouse models that the macrophage iron depletion seen in iron deficiency may have pro-inflammatory effects (Pagani *et al*., 2011). Systemic iron homeostasis is predominantly regulated by the liver where the expression of TfR2 constitutes an important systemic iron sensor regulating the production of pro-inflammatory hormones

such as hepcidin. The modulation of pro-inflammatory profiles in hepatocytes and macrophages has been suggested as effective approaches for intervention in obesity (Kheder *et al*., 2016). Increased understanding of these dynamics may allow us to target potentially harmful populations whilst promoting anti-inflammatory or restorative populations to ultimately guide the development of effective treatment strategies.

PPARγ plays a key role in maintaining, among other, insulin-mediated signalling and glucose homeostasis. Thus, the important role attributed to PPARγ in substrate fractionation towards energy expenditure or accumulation is crucial to promote insulin resistance and overweight/obesity development. As such, ChB-induced PPARγ overexpression can be associated to increased energy expenditure that together with the decreased GI allow to hypothesize a normalized insulin sensitivity and down-regulated lipogenesis, but improved fat partitioning and metabolism.

5. CONCLUSIONS

The inclusion of flour from chia (*Salvia hispanica* L.) at 5% exerts beneficial effects decreasing glycaemic index and promoting immunonutritional changes with a preventive role in glucose tolerance and a number of components of the metabolic syndrome.

ACKNOWLEDGMENTS

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FIGURE CAPTIONS

Figure 1. Mean (n = 5) typical profile of blood glucose concentrations in rats fed with bread formulations prepared by inclusion of flour from chia (5%, ChB), whole wheat (WWB) or white wheat (WB).

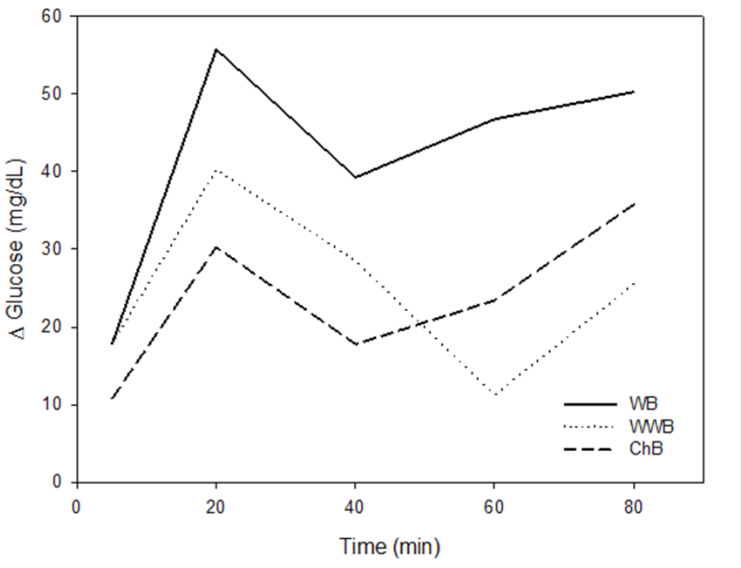

Figure 2. Area under the curve (AUC), hydrolysis index (HI) and estimated glycemic index (GI) of chia-containing bread formulation in comparison to whole wheat (WWB) and white bread (WB). Results are expressed as mean ± SD (n = 5). Different superscript letters indicate statistical (P<0.05) differences.

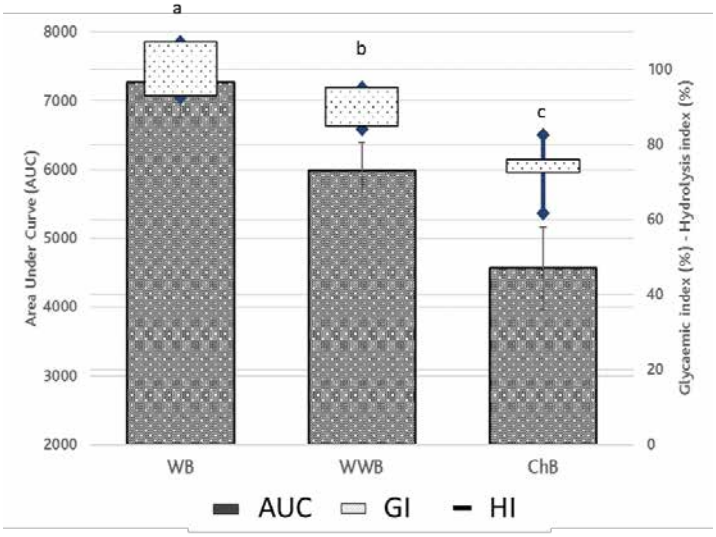

Figure 3. Fold change in the hepatic expression (mRNA) of transferrin receptor 2 (TfR2) and the peroxisome proliferator-activated receptor gamma (PPARγ) in animals fed with a chia-containing bread formulation (ChB), a whole wheat (WWB) or white bread (WB). Results are expressed as mean ± SD (n = 5). Different superscript letters indicate statistical (P<0.05) differences for each individual parameter in relation to WB.