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# Whole sorghum flour improves glucose tolerance, insulin resistance and preserved pancreatic islets function in obesity diet-induced rats

Érica Aguiar Moraes <sup>a</sup>, Rafaela da Silva Marineli <sup>a</sup>, Sabrina Alves Lenquiste <sup>a</sup>, Valéria Aparecida Vieira Queiroz <sup>b</sup>, Rafael Ludemann Camargo <sup>c</sup>, Patricia Cristine Borck <sup>c</sup>, Everardo Magalhães Carneiro <sup>c</sup>, Mário Roberto Maróstica Júnior <sup>a,\*</sup>

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#### ABSTRACT

The effects of sorghum flour fractions (whole and decorticated flours and bran) were evaluated for oxidative stress and obesity parameters in diet-induced obese rats. Compared to high fat-fructose groups, sorghum flour fractions reduced liver fat and whole sorghum flour decreased fasting glucose, improved glucose tolerance, insulin resistance and reduced insulin secretion. Sorghum showed a slight improvement in antioxidant status. Animals fed with sorghum flour fractions improved liver CAT, GRd and GPx activities and decreased plasma lipid peroxidation. Additionally, whole sorghum flour can be used as a strategy to ameliorate glucose/insulin homeostasis by increasing insulin sensitivity, leading to pancreatic islet function preservation in a prediabetic condition.

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E-mail address: mario@fea.unicamp.br (M.R. Maróstica Júnior).

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<sup>&</sup>lt;sup>a</sup> Department of Food and Nutrition, Faculty of Food Engineering, University of Campinas, SP, Brazil

<sup>&</sup>lt;sup>b</sup> Embrapa Maize & Sorghum, Brazilian Agricultural Research Corporation, Sete Lagos, MG, Brazil

<sup>&</sup>lt;sup>c</sup> Department of Structural and Functional Biology, Institute of Biology, University of Campinas, SP, Brazil

<sup>\*</sup> Corresponding author.

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#### 1. Introduction

Obesity is a worldwide public health problem. In 2014, more than 1.9 billion adults were overweight and over 600 million were obese (WHO, 2015). As a multifactorial development disease, the excess of food intake, in mainly high-fat and high-fructose diets, has been related to an increase in the prevalence of obesity (Deer, Koska, Ozias, & Reaven, 2015; Samuel, 2011). Excessive caloric intake has been also suggested to increase oxidative stress in different tissues and depletion of antioxidant enzymes and reduced glutathione levels (Marineli et al., 2015; Noeman, Hamooda, & Baalash, 2011). Weight gain and oxidative stress are major risk factors for the development of insulin resistance, glucose intolerance, type 2 diabetes mellitus, atherosclerosis, chronic low-grade inflammatory state and non-alcoholic fatty liver disease (Deer et al., 2015; Wang et al., 2014).

Diet modification is a crucial strategy for intervention against obesity and associated diseases. Increasing whole grain intake has been considered an important role as a dietary strategy for reducing the development risks of those diseases. Beneficial effects of whole grain are associated to phenolic compound contents as well as dietary fiber (Poquette, Gu, & Lee, 2014; Wang et al., 2014). Sorghum grain composes this background with specific phenolic compound groups such as luteolinidin and apigeninidin, condensed tannin as well as dietary fibers, such as resistant starch and β-glucan (Dunn, Yang, Girard, Bean, & Awika, 2015; Moraes et al., 2015; Shen, Zhang, Dong, Ren, & Chen, 2015). Recent studies have demonstrated that these compounds display a regulator key role in glucose homeostasis and insulin secretion, as well as cholesterollowering effects, reducing adiposity, improving antioxidant status and decreasing oxidative and low-grade inflammation biomarkers (Khan, Yousif, Johnson, & Gamlath, 2015; Kim, Kim, & Park, 2015; Moraes et al., 2012; Poquette et al., 2014; Shen et al., 2015).

Sorghum studies have focused on the use of whole flour, phenolic extract and decorticated flour (Kim & Park, 2012; Moraes et al., 2012; Shen et al., 2015). Nevertheless, sorghum abrasive processes produce decorticated grains and bran, which have different approximate compositions, phenolic compounds and dietary fiber content (Awika, McDonough, & Rooney, 2005; Moraes et al., 2015). Additionally, our previous study demonstrated that sorghum bran contains higher amounts of phenolic compounds, antioxidant capacity, dietary fiber and has a lower estimated glycemic index in comparison to decorticated sorghum flour (Moraes et al., 2015). It may suggest that different metabolic outcomes may be achieved with sorghum flour fraction intake. Thus, we hypothesized that diets containing sorghum flour fractions with different phenolic and dietary fiber features could reduce obesity and associated disease risk factors in rats fed with a high fatfructose diet. Therefore, this study aimed to evaluate the effects of whole sorghum flour (WSF), decorticated sorghum flour (DSF) and sorghum bran (SB) on oxidative stress and obesity parameters in diet-induced obese rats.

#### 2. Material and methods

#### 2.1. Sorghum sample

Sorghum SC 21 genotype with brown pericarp and pigmented testa (condensed tannins), previously selected among 100

genotypes due to its high antioxidant capacity, was grown in the experimental field of Embrapa Maize and Sorghum, Sete Lagoas, MG, Brazil, in February 2012. Experimental plots were composed of two, three meter rows, with a spacing of 0.50 m between rows. The fertilization at planting consisted of an application of 300 kg·ha<sup>-1</sup> of formulated 08-28-16 (NPK). After 25 days of planting, fertilization with 50 kg·ha<sup>-1</sup> of nitrogen was performed. Whole sorghum flour (WSF) and the decortication process to obtain decorticated sorghum flour (DSF) and sorghum bran (SB) were described by Moraes et al. (2015) such as the approximate composition of each flour.

#### 2.2. Sample extraction, total phenolics and antioxidant activities

Total phenolic content was measured by the Folin-Ciocalteu method (Singleton, Orthofer, Lamuela-Raventós, & Lester, 1999). Antioxidant activities were determined by the following assays: (1) Oxygen radical absorbance capacity test (ORAC) (Dávalos, Gómez-Cordovés, & Bartolomé, 2004); (2) 2,2-azinobis (3-ethylben zothiazoline-6-sulfonate) radical cation (ABTS) (Miller, Rice-Evans, Davies, Gopinathan, & Milner, 1993); (3) 2,2-diphenyl-1picrylhydrazyl (DPPH) (Awika, Rooney, Wu, Prior, & Cisneros-Zevallos, 2003; Herald, Gadgil, & Tilley, 2012) and (4) Ferric reducing antioxidant power (FRAP) (Benzie & Strain, 1996). Samples of 0.5 g were extracted in 10 mL of acetone: water 70:30 (v/v) for 2 h under mechanical shaking at low speed (Marconi®). Then it was stored at -20 °C in the dark, overnight. Samples were equilibrated at room temperature and centrifuged at 2790g for 10 min. Sample residues were rinsed with two additional 10 mL volumes of solvent with further shaking for 5 min, then centrifuged at 2790g for 10 min. The three aliquots were mixed and stored at -20 °C in the dark until the analysis was performed within 24 h (Awika et al., 2005). All extractions and analyses were conducted in triplicate.

### 2.3. Animals and experimental diets

This work was approved by the Ethics Commission on Animal Use (CEUA/ UNICAMP) protocol no. 3003-1. Forty (20 -23-dayold) male Wistar rats obtained from the Multidisciplinary Center for Biological Investigation, University of Campinas. The rats were kept in individual cages for growth under controlled conditions  $(22 \pm 1 \, ^{\circ}\text{C}, 60-70\% \text{ humidity}, 12 \text{ h light/dark cycle})$  and had free access to water and chow diet for 4 weeks. After growing, the animals were separated by weight (185.01 g ± 11.23) and assigned to one of five diets (n = 8/group) for 12 weeks. Experimental diets were formulated from purified ingredients according to the American Institute of Nutrition (Reeves, Nielsen, & Fahey, 1993) with a protein concentration of 12% (AIN-93M). A lean control group was fed with AIN-93M diet; the high fat-fructose group (HFF) received a diet containing 4% (w/w) soybean oil, 31% (w/w) lard and 20% fructose (w/w) (Marineli et al., 2015). The sorghum diet groups received HFF diet added to whole sorghum flour (HFF-WSF), decorticated sorghum flour (HFF-DSF) or sorghum bran (HFF-SB). Whole sorghum flour and sorghum bran were added to diets in sufficient amounts to provide 100% of the dietary fiber recommendation (5% of cellulose fiber); and decorticated sorghum flour replaced all corn starch (13.08 g·100 g<sup>-1</sup>) (Table 1). Diets were prepared monthly, packed in dark polyethylene bags and

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