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Coffee silverskin potential in the prevention of metabolic syndrome: Effects upon Caco-2, HepG2, and 3T3-L1 cells

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Introduction

Metabolic syndrome (MetS) is as a cluster of metabolic dysregulations that includes insulin resistance, hyperglycemia, hypertension, dyslipidemia, and central obesity [1,2]. This condition currently affects approximately 25% of the global population, is characterized by a pro-inflammatory state driven by abnormal glucose metabolism, and significantly increases the risk of type 2 diabetes, cardiovascular disease, and cancer [1,2]. The protective effects of coffee on MetS through antidiabetic, anti-inflammatory, and antiadipogenic effects have been extensively described in the literature [3]. Considering the need to find sustainable solutions for the great amounts of coffee by-products generated every year in the coffee chain, allied to the need to find alternative food sources with potential health benefits, namely in the context of MetS, this study aimed to investigate the potential anti-MetS effect of coffee silverskin (CS), the major by-product of coffee roasting industries, having in view its valorization and the development of functional foods.

Samples and methodologies

Preparation of an aqueous extract by Ultrassound-assisted extraction [4]

Coffee silverskin (CS)

6 g ground sample/300 mL H_2O, 10 min

↓

Filtration

↓

Freeze-dry (-80 °C, 0.015 mbar)

Evaluation of anti-MetS effects of CS extract (24 h exposure) on enterocytes (Caco-2 cells), hepatocytes (HepG2 cells), and adipocytes (3T3-L1 cells)

1) Effects on sugar uptake

Quantification of ^{3}H-D-glucose (^{3}H-DG) uptake in Caco-2, HepG2, and 3T3-L1 cells and quantification of ^{14}C-fructose (^{14}C-FRU) uptake in Caco-2 and HepG2 cells by liquid scintillation counting [4]

2) Effects on gene expression of relevant genes involved in sugar and lipid metabolism

Quantification of mRNA levels by RT-q-PCR [1]:

- Caco-2 cells: SGLT1 (Sodium-glucose linked transporter 1), GLUT2 (Glucose facilitative transporter 2), and GLUT5 (Glucose facilitative transporter 5) (sugar metabolism)
- HepG2 cells: GK (glucokinase), GLUT2 and GLUT5 (sugar metabolism); ACC1 (Acetyl-CoA carboxylase 1) and FAS (Fatty acid synthase) (lipid metabolism); SREBP-1c (Sterol regulatory element-binding protein 1c) and chREBP (Carbohydrate-responsive element-binding protein-1) (glucose and lipid metabolism)

3) Anti-inflammatory effects

Quantification of NO (nitric oxide) and NAG (N-acetylglucosamine) levels in Caco-2, HepG2, and 3T3-L1 cells by spectrophotometric assays [1]

Results and discussion

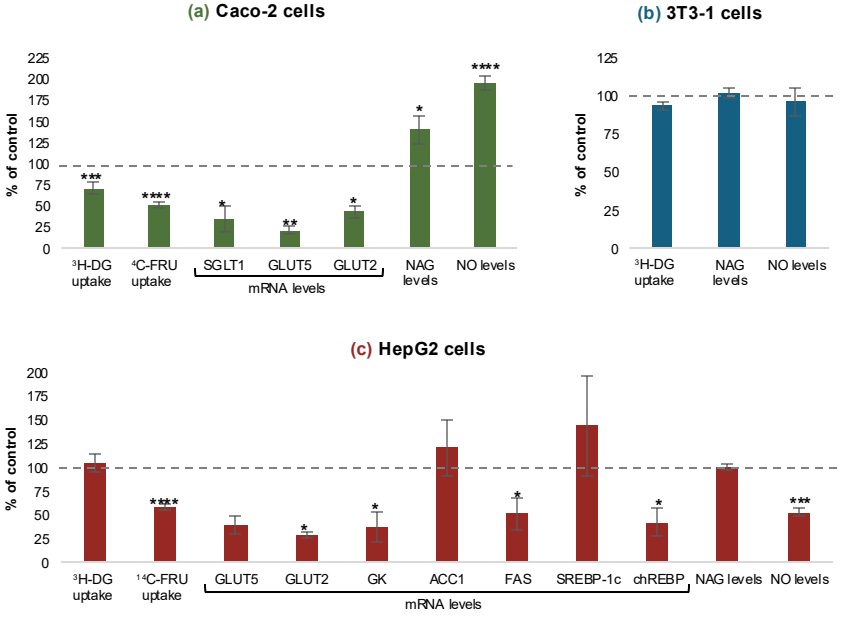

Figure 1. Effects of CS extract (CSE) on sugar (^{3}H-DG and ^{14}C-FRU) uptake, gene expression (mRNA levels) of relevant genes involved in sugar (SGLT1, GLUT5, GLUT2 and GK) and lipid (ACC1, FAS, SREBP-1c, and chREBP mRNA levels) metabolism, and on inflammatory marker (NAG and NO) levels in **(a)** Caco-2, **(b)** 3T3-L1, and **(c)** HepG2 cells (n = 5–8). CSE was tested at 1 mg/mL in Caco-2 cells and at 0.01 mg/mL in HepG2 and 3T3-L1 cells in order to mimic an *in vivo* scenario. Results on gene expression are expressed as the expression of the gene (e.g., GLUT2) relative to β-actin. Data show arithmetic means ± S.E.M. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$ vs. control, by Student's *t*-test.

- CSE significantly reduced ^{3}H-DG and ^{14}C-FRU uptake by Caco-2 cells, as well as gene expression of sugar transporters (GLUT2, GLUT5, and SGLT1), while in HepG2 cells, it significantly reduced ^{14}C-FRU uptake and GLUT2 gene expression → **CSE reduced intestinal sugar absorption, and decreased fructose removal by the liver**
- In HepG2 cells, CSE significantly reduced gene expression of some key genes involved in glucose (GK) and lipid (FAS and chREBP) metabolism → **CSE revealed hepatic antiadipogenic potential**
- CSE significantly decreased NO levels in HepG2 cells, but it also significantly increased NO and NAG levels in Caco-2 cells → **CSE displayed different inflammatory effects (anti- vs pro-inflammatory effects) depending on cell line**
- CSE did not present any effects on 3T3-L1 cells

Conclusions & Perspectives:

CS presented promising anti-MetS potential *in vitro*, opening the possibility of further *in vivo* and clinical trials studies to validate these results and develop a functional food containing this coffee by-product.

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