



Abstract

# Influence of Coffee Silverskin, Caffeine and 5-Caffeoylquinic Acid on Sugar Uptake Using Caco-2 Cells: A Preliminary Study <sup>†</sup>

Juliana A. Barreto Peixoto <sup>1</sup>, Nelson Andrade <sup>1,2</sup>, Susana Machado <sup>1</sup>, Anabela S. G. Costa <sup>1</sup>,  
Maria Beatriz P. P. Oliveira <sup>1</sup>, Fátima Martel <sup>2,3</sup> and Rita C. Alves <sup>1,\*</sup>

<sup>1</sup> REQUIMTE/LAQV, Department of Chemical Sciences, Faculty of Pharmacy, University of Porto, 4050-313 Porto, Portugal; jpeixoto@ff.up.pt (J.A.B.P.); nelsonandrade@outlook.com (N.A.); su\_tche@hotmail.com (S.M.); acosta@ff.up.pt (A.S.G.C.); beatoliv@ff.up.pt (M.B.P.P.O.)

<sup>2</sup> Unit of Biochemistry, Department of Biomedicine, Faculty of Medicine, University of Porto, 4200-319 Porto, Portugal; fmartel@med.up.pt

<sup>3</sup> Instituto de Investigação e Inovação em Saúde (I3S), University of Porto, 4200-135 Porto, Portugal

\* Correspondence: rcalves@ff.up.pt

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**Abstract:** Coffee silverskin (CS) is the major by-product of coffee roasting and a source of caffeine and chlorogenic acids (CGA), recognized modulators of sugar metabolism. In this work, the effect of a CS extract on glucose and fructose uptake by human intestinal epithelial (Caco-2) cells was ascertained. Freeze-dried aqueous extracts were prepared using an ultrasound probe. The obtained powder was characterized regarding its caffeine content and CGA profile by RP-HPLC-DAD. Caco-2 cells were incubated (at 37 °C for 24 h) with 1 mg/mL of extract, and then glucose and fructose uptake were measured by incubating the cells (at 37 °C for 6 min) with 10 nM <sup>3</sup>H-deoxy-D-glucose (<sup>3</sup>H-DG) or 100 nM <sup>14</sup>C-fructose (<sup>14</sup>C-FRU), respectively. The effects of the major compounds identified were similarly assessed using standards, individually and combined. Furthermore, the mRNA levels of the intestinal transporters of these sugars (SGLT1, GLUT2, and GLUT5) were quantified by RT-qPCR after cell treatment (for 24 h) with the CS extract. Caffeine was the main component of the extract and 5-caffeoylquinic acid (5-CQA) was the major CGA, followed by 5-feruloylquinic acid (5-FQA). Other isomers were found in minor amounts (3-CQA, 4-CQA, and 4-FQA). CS was able to significantly reduce <sup>3</sup>H-DG and <sup>14</sup>C-FRU uptake (~17% and ~19%, respectively). These effects were not related to cytotoxicity, as confirmed by the lactate dehydrogenase assay. When testing individual compounds at the concentrations present in the extract, neither caffeine nor 5-CQA influenced <sup>3</sup>H-DG and <sup>14</sup>C-FRU uptake, but significant inhibitions were found when the compounds were combined together (~16% and ~18%, for <sup>3</sup>H-DG and <sup>14</sup>C-FRU uptake, respectively). This synergistic activity suggests their major role in CS effects. The extract also decreased (in 71%) the expression levels of the GLUT2 transporter, without any influence on the SGLT1 and GLUT5 transporters, thus evidencing the importance of GLUT2 on sugar uptake results. Overall, these findings highlight the beneficial effects that CS might have on type 2 diabetes and other metabolic disorders.

**Keywords:** silverskin; chlorogenic acids; caffeine; HPLC-DAD; intestinal sugar uptake; Caco-2 cells



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