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Cagaita fruit (*Eugenia dysenterica* DC.) and obesity: Role of polyphenols on already established obesity

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ABSTRACT

Polyphenol-rich cagaita (*Eugenia dysenterica* DC.) extracts (PCE) have previously shown to prevent body weight and adiposity induced by high-fat/high-sucrose (HFS) diet. Whether PCE also exerts protective effects in already developed obesity is unknown. In order to test this hypothesis, male C57BL/6J obese mice (previously feed with a HFS diet for six weeks) were treated with PCE at two doses, 7 mg gallic acid equivalent (GAE)/kg body weight (PCE I group), and 14 mg GAE/kg body weight (PCE II group) or water (HFS and Chow groups) by oral gavage for eight weeks. PCE did not affect body weight and adiposity of obese mice. However, PCE did protect against dyslipidemia, fasting hyperglycemia, and glucose intolerance, and attenuated both hepatic gluconeogenesis and inflammation as observed by the expression of tumor necrosis factor-α and transcriptional factor NF-κB. These results indicate that PCE improves glucose homeostasis of obese mice by attenuating hepatic gluconeogenesis and inflammation.

1. Introduction

Polyphenols are plant-derived compounds widely known for their antioxidant and anti-inflammatory properties associated to health benefits in humans (Gorlach, Fichna, & Lewandowska, 2015). Dietary polyphenols seem to also exert anti-inflammatory and/or antioxidant effects in obesity-associated diseases. An important strategy to deal with obesity-associated complications is decreasing oxidative stress and levels of reactive oxygen species (ROS) (Wang et al., 2014). ROS represent one of many factors that have been implicated in the development of insulin resistance, as strongly supported by the extensive association among markers of oxidative stress, obesity and diabetes (Houstis, Rosen, & Lander, 2006). Therefore, polyphenols may have antiobesity and antidiabetic benefits due to their ability to act as antioxidants and singlet oxygen quenchers, therefore attenuating the deleterious effects of exacerbated ROS production, as well as obesity-associated inflammation (Wang et al., 2014). Noteworthy, polyphenols exhibit biological activities far beyond their antioxidative action (Gorlach et al., 2015), modulating different intracellular signaling cascades implicated in cell growth, proliferation and apoptosis (Crozier, Jaganath, & Clifford, 2009).

The complexity of obesity and associated diseases presents numerous challenges but also several opportunities for therapeutic intervention (Rosen & Spiegelman, 2014). In this sense, plant-derived compounds including polyphenols have been shown, when consumed as a part of a regular and balanced diet, to exert beneficial effects against the development of obesity and associated abnormalities. These antioxidant, antiobesity, and antidiabetic properties of polyphenols are being investigated by many pharmaceutical and food companies aiming the development of products to help fighting the health problems resulting from an increasingly overweight population (Granato, Alezandro, & Nazzaro, 2015).

Tropical countries have a complex flora composed of a large amount of native and exotic fruit species, for which limited information on potential functional properties is available. The investigation of such properties may be of interest to the pharmaceutical and food industries (Costa, Garcia-Diaz, Jimenez, & Silva, 2013). Cagaita (*Eugenia dysenterica* DC.) is a Brazilian Cerrado biome tree whose fruit and leaves are used as alternative medicine by local communities to treat diarrhea, diabetes, and jaundice (Lima et al., 2011). Chemical characterization revealed that cagaita fruit is a source of vitamin C and polyphenols (Cardoso, Martino, Moreira, Ribeiro, & Pinheiro-Sant'Ana, 2011; Gonçalves, Lajolo, & Genovese, 2010). Recently, we have shown that polyphenol-rich cagaita extract (PCE) contains high amounts of tannins

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