Research Article

Cocoa polyphenols treatment ameliorates visceral obesity by reduction lipogenesis and promoting fatty acid oxidation genes in obese rats through interfering with AMPK pathway

Faisal Ali[1], Amin Ismail[1], Norhaizan Mohd Esa[1,2] and Chong Pei[3]

[1] Department of Nutrition and Dietetics, Metabolism and Genomics Group, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Selangor, Malaysia
[2] Laboratory of Molecular Biomedicine, Institute of Bioscience, Universiti Putra Malaysia, Selangor, Malaysia
[3] Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Selangor, Malaysia

This study was conducted to investigate the pharmacological activity of cocoa polyphenols (CPs) on visceral obesity markers and the possible mechanisms. In this study, Sprague–Dawley (SD) rats were fed either a low-fat diet (LFD) or a high-fat diet (HFD). After 12 wk of diet intervention, only one group of HFD rats ($n = 10$/group) were treated at a dose of 600 mg/kg bw/day CPs (HFD + CPs) for 4 wk. The gene and protein expression levels of phosphorylation of AMPK-activated protein kinase α/β (AMPK α/β) were measured using real time-PCR and Western blotting. The mRNA expression of lipogenic key enzymes (Acaca, Fasn, Mcat, and Scd-1), and β-oxidation key enzymes (CPT1, Prkaa1, Acox1) were investigated. In addition, the upstream transcription factors (PPARα, PPARγ, C/EBPα, and SREBP-1c) were also examined. In accordance with these findings, CPs treatment improved visceral adiposity, adipocytes hypertrophy, and liver steatosis. AMP-activated protein kinase α/β (AMPK α/β) phosphorylation in liver and adipose tissue of HFD + CPs-treated rats was activated compared with HFD-fed rats. The expression of lipogensis related-genes was decreased, while expression levels of β-oxidation-related genes were increased compared with HFD-fed rats. Together, these data partially unravel the ameliorative effects of CPs treatment on visceral obesity markers by inhibiting lipogenesis and promoting β-oxidation related-genes through activation of the AMPK pathway.

Practical applications: There is a metabolic logic linking the expended visceral or abdominal fat depot to dyslipidemia. The conceivability of using a natural dietary supplement to regulate lipid metabolism homeostasis is appealing as this by product of the defatted cocoa juice industry is non-toxic, cheap, and has shown hypolipidemic properties. This is essentially significant in the context of the rising costs of obesity and its related diseases care. The ability of polyphenolics to suppress SREBP-1c, the target of statins, while activating PPARα, the target of fibrates, suggest it can naturally find its role in the treatment of hyperlipidemia.

Keywords: AMPK pathway / Cocoa polyphenols / Fatty acid β-oxidation genes / Lipogenesis genes / Visceral obesity

Received: November 6, 2014 / Revised: May 26, 2015 / Accepted: June 12, 2015

DOI: 10.1002/ejlt.201400581

Correspondence: Dr. Faisal Ali, Department of Nutrition and Dietetics, Metabolism and Genomics Group, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Selangor 43400, Malaysia
E-mail: sshrmany@yahoo.co.uk
Fax: +60 389426769

Abbreviations: cDNA, complementary deoxyribonucleic acid; **CMC,** carboxymethyl cellulose; **CPs,** cocoa polyphenols; **FFAs,** free fatty acids; **GAPDH,** glyceraldehyde-3-phosphate dehydrogenase; **HFD,** high fat diet; **LFD,** low fat diet; **MES-WAT,** mesenteric white adipose tissue; **mRNA,** messenger ribonucleic acid; **NCBI,** National Center for Biotechnology Information; **PPARs,** peroxisome proliferator-activated receptors; **qRT-PCR,** quantitative real-time polymerase chain reaction; **SD,** Sprague–Dawley; **TC,** total cholesterol; **TG,** triglyceride

1 Introduction

Visceral obesity is a growing global disease that usually develops from excessive fat storage and adiposity of mesenteric adipose tissue. Because obesity is accounted as a major risk factor for most metabolic diseases, including dyslipidemia, type 2 diabetes, hypertension, and cardiovascular disease, many studies have been conducted to disclose the main components in energy homeostasis, which is critical to develop therapeutic agents for obesity and obesity-associated metabolic diseases [1–3]. A group of transcription factors such as peroxisome proliferator-activated receptor γ

