Mol Cell Biochem (2014) 385:257–264
DOI 10.1007/s11010-013-1834-0

Inhibitory effects of baicalin in the early stage of 3T3-L1 preadipocytes differentiation by down-regulation of PDK1/Akt phosphorylation

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Received: 12 July 2013 / Accepted: 26 September 2013 / Published online: 4 October 2013

Abstract Baicalin is a flavonoid derived from the root of *Scutellaria baicalensis* and exhibits a broad spectrum of biological activities including anti-adipogenesis. However, the inhibitory role of baicalin in the early stage of 3T3-L1 adipocyte differentiation relevant to the signaling upstream of peroxisome proliferator-activated receptor-γ (PPAR-γ) and CCAAT/enhancer binding proteins (C/EBPs) expression is unclear, and is the subject of the present investigation. We used 3T3-L1 preadipocytes for adipocyte differentiation, Oil Red-O staining for the intracellular lipid accumulation assay, and real-time polymerase chain reaction (RT-PCR) for assaying the expression of major adipocyte transcription factors. We found that baicalin markedly suppressed the Akt phosphorylation in early stage of adipocytes differentiation. In addition, we observed that baicalin and LY294002 (as an inhibitor of Akt phosphorylation) significantly inhibited adipocyte differentiation by down-regulating several adipocyte-specific transcription factors, including PPAR-γ and C/EBPs in 3T3-L1 preadipocytes. Furthermore, we observed that baicalin significantly suppressed the Akt phosphorylation by inhibiting phosphoinositide-dependent kinase 1 (PDK1). These results indicate that the anti-adipogenesis effect of baicalin involves down-regulation of major transcription factors in 3T3-L1 adipocyte differentiation including PPAR-γ, C/EBP-β, and C/EBP-α through the down-regulation of PDK1/Akt phosphorylation.

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Keywords Baicalin · 3T3-L1 cells · Anti-adipogenesis · Phosphorylation · PDK1/Akt pathway

Introduction

Obesity is characterized by adipogenesis, the differentiation process of preadipocytes into adipocytes, which plays a pivotal role in fat metabolism [1]. The 3T3-L1 mouse preadipocyte cell line has been commonly used to investigate the molecular mechanism of adipogenesis as an in vitro model system [2]. The 3T3-L1 preadipocytes differentiated into adipocytes and express adipocytes-specific genes in the presence of adipogenic cocktail, containing 3-isobutyl-1-methylxanthine (IBMX), dexamethasone (Dex), and insulin which are commonly abbreviated MDI [3]. Peroxisome proliferator-activated receptor–gamma (PPAR-γ), CCAAT/enhancer binding protein beta (C/EBP-β), and CCAAT/enhancer binding protein alpha (C/EBP-α) are the major transcription factors expressed during adipogenesis in 3T3-L1 preadipocytes [4, 5]. These major transcription factors together activate the expression of adipocyte-specific genes including adiponectin, lipoprotein lipase (LPL), adipocyte fatty acid-binding protein 2 (aP2), and fatty acid synthase in adipogenesis [6–8].

Several studies have reported that the extracellular signal-regulated kinase 1/2 (ERK1/2) and Akt pathways play pivotal roles in adipogenesis [9, 10]. Inhibition of the ERK pathway in the early stage of differentiation would block adipogenesis [11]. For example, epigallocatechin gallate inhibits adipocyte differentiation by suppression of ERK 1/2 phosphorylation in 3T3-L1 preadipocytes [12]. Previous studies have reported that mouse embryonic fibroblasts lacking Akt failed to differentiate into mature