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Effects of fisetin on mouse lipid metabolism in vitro and in vivo

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ABSTRACT:

Objective: The aim of this study was to investigate the anti-obesity effects of the polyphenol fisetin in 3T3-L1 preadipocytes and C57BL/6 female mice that were fed a high-fat diet (HFD).

Background: Polyphenols, such as sakuranetin, hesperetin, tea catechin, and quercetin, reportedly regulate adipocyte differentiation in 3T3-L1 cells. Furthermore, green tea, apple, and molokheiya polyphenols exhibit anti-obesity activities in HFD-treated obese rats or mice. Fisetin is abundant in plants, fruits, and vegetables and exhibits multiple biological activities, such as the inhibition of prostate cancer growth, neuroprotection, and protection against osteoporosis. In addition, fisetin regulates obesity by targeting mammalian target of rapamycin complex 1 signaling, which is a central mediator of lipid biosynthesis.

Materials and methods: (1) *in vitro* experiments; we investigated the effects of fisetin on intracellular lipid accumulation and glycerol-3-phosphate activity during the differentiation of 3T3-L1 cells. We monitored expression of adipogenetic related-genes in 3T3-L1 cells by real-time polymerase-chain-reaction. (2) *in vivo* experiments; we examined the effects of fisetin on anti-obesity activities in C57BL/6 female mice that were fed a HFD.

Results: Fisetin inhibited intracellular lipid accumulation and glycerol-3-phosphate activity during the differentiation of 3T3-L1 cells in a dose-dependent manner (50-75 μM). In addition, real-time polymerase-chain-reaction revealed that this compound suppressed the expression of peroxisome proliferator-activated receptor γ (PPARγ), adipocyte protein 2, and perilipin mRNAs in 3T3-L1 cells. In contrast, anti-obesity activities, such as reduction of body weight and fat tissue, and improvements in obesity-related blood biochemical parameters and fatty liver, were not observed in HFD-induced mice treated with fisetin (20 mg/kg body weight) by intraperitoneal injections twice per week for 8 weeks.

Conclusions: Fisetin exerted anti-adipogenic activities by inhibiting the expression of PPARγ mRNA in 3T3-L1 preadipocytes. However, fisetin (20 mg/kg body weight) did not affect HFD-induced obesity. Our findings indicated that fisetin could be used as an effective remedy in the treatment of the symptoms of obesity.

Keywords: Fisetin, MC3T3-L1 cells, Fatty accumulation, PPARγ, Obesity, Anti-obesity activity